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ERRATA.

Vol. 32, No. 4, p. 246, BEQUAERT's summary, line 3 of title, for Blandfordia read Blanfordia, and for H. A. PILSBURY read H. A. PILSBRY. Also in text of summary read Blanfordia for Blandfordia throughout.

Regarding the summary of the article by MATHIS, LAIGRET & DURIEUX (pages 284–285), the authors have written saying that the statement regarding the occurrence of yellow fever after vaccination has been misinterpreted ; consequently the last 3 lines of the abstract should be deleted.

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 32.] 1935. [No. 1.

BERIBERI AND EPIDEMIC DROPSY.

AALSMEER (W. C.). Bijdrage tot de pathogenese der beri-beri. [**Contributions to the Pathogenesis of Beriberi. Parts I, II & III.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. May 8. Vol. 74. No. 10. pp. 582–589; June 19. No. 13. pp. 776–782; July 3. No. 14. pp. 862–874. With 2 charts.

I. *Primary Beriberi due to B Avitaminosis.*—All the author's publications make special reference to the adrenalin test and its use as an indicator of the stage of the disease or the reality of cure and of the value of the therapeutic measures adopted. This test, it will be remembered, depends on the influence of adrenalin injections in active beriberi upon the diastolic blood pressure which is called, alternatively, the minimum tone pressure because it is the pressure registered by the sphygmometer at the moment when the auscultatory tone or bruit disappears with decompression of the brachial artery. Sometimes in beriberi an auscultatory murmur is already present before application of the recording instrument. In such cases, of course, the murmur cannot disappear with relaxation of pressure on the artery and the diastolic pressure is consequently registered as zero or nearly zero. No adrenalin test can be applied at all in such circumstances. But the essence of the test is that, when some diastolic pressure is registered, the administration of adrenalin in a hypodermic dose of 1 mgm. will, if observations are taken at five minute intervals, bring that pressure down to the zero point in an uncured case of beriberi. That is to say, the auscultatory murmur will persist even on complete relaxation of the pressure on the artery, as long as the patient is under the influence of adrenalin. This action of the adrenalin is due primarily to its effect on the heart itself but also to its dilating effect upon the peripheral blood vessels. The sum total of the different factors concerned is described under the word "gradient," expressing the fact that the rapidity of development of the fall in diastolic blood pressure and an unstable wave front are the most important factors concerned in this vascular syndrome.

By means of this test, then, Aalsmeer has been able to gauge the value of various dietaries, the interference of food substances themselves with vitamin absorption and the rôle which intestinal disturbance can play in the development of beriberi. Other influences, such as the psychic condition of the patient, may be determining factors in

preventing the disappearance of symptoms with the administration of vitamin B. This was the verdict in the case of prisoners on the island of Onrust, Java [this *Bulletin*, Vol. 31, p. 477].

There are other diseases than beriberi in which the weak tones of decompression take long to disappear or fail to disappear. Such diseases for example are exophthalmic goitre, aortic insufficiency and severe anaemias. The occurrence of this phenomenon in BASEDOW'S disease suggests that thyroid dysfunction or a pluriglandular syndrome may be at the root of some of the symptomatology of B-avitaminosis.

In certain cases the inoculation of adrenalin in a sufferer from beriberi failed to give rise to tone formation at low or zero diastolic pressures, a phenomenon attributable to decompensation of the left heart. The administration then of a preliminary injection of cardiazol was necessary to bring about stimulation of the heart, after which the adrenalin test became positive.

The methods referred to in this article have been tested out on patients. Such patients were in the first place given complete rest in bed and still kept on a vitamin-poor diet. The diastolic blood pressure, even if it were zero on admission, usually rose as the result of the simple rest in bed and this allowed of the application of the adrenalin test. A test case will illustrate the results obtained :—On admission the patient's diastolic pressure was zero. Even after five days' rest in bed it still remained zero. With the addition, however, of red rice to the vitamin-poor dietary for 8 days the pressure rose to 60. Then the adrenalin test was applied and the successive minimal diastolic pressures, at the usual five minute intervals, became 60, 50, 50, 50, 40, 0. That is to say zero pressure was again reached and the deduction could be made that the patient was not yet cured and his beriberi still remained active. After 15 days of a red rice dietary the improvement seen became a permanent one and the adrenalin test showed figures of 65, 65, 65, 65, 65, 65, or no diminution of diastolic pressure at all ; repetition on the following day gave values 80, 75, 75, 70, 60, 70.

Besides red rice and Katjang idjoe a preparation of vitamin B, in tablet form or in ampoules containing liquid, may be equally effective for cure.

II. *Secondary Beriberi due to Disturbance of Intestinal Function.*—Although the administration of vitamin B should effect a cure in beriberi it is not the case that all or any vitamin-containing food will serve the purpose. This may be illustrated from actual cases and the test of the result should be the fall or absence of fall to zero of the diastolic pressure with the administration of adrenalin. A patient who was admitted to hospital and left for 7 days on vitamin-poor diet had a minimal diastolic pressure of 40. The adrenalin test brought this pressure down to zero. He was next placed for 6 days on red rice, dedek and tempe. Once more the adrenalin test brought the pressure to zero. And so it was with the addition of yeast. Purgation and 3 days of milk diet, with the idea of correcting gastro-intestinal disturbance, followed again by vitamin-poor food plus yeast gave a much improved adrenalin test as shown by the figures 65, 65, 40, 40, 40. This single example, out of the many given by the author, is intended to show that in spite of sufficient vitamin containing food avitaminosis can still remain, which may be due especially to disturbance of the intestinal functions (enterogenic beriberi). There are even cases in which none of the usual methods of feeding and not

even vitamin tablets themselves are successful. When patients then are treated by purgation or receive a milk diet for some days to promote normal intestinal functioning one may, as in the case of the patient mentioned, find that a return to the old vitamin-containing diet is effective. Again it may be found that withdrawal of red rice from the diet is promptly effective, presumably because the dietary contained an excess of carbohydrate. Place alongside these observations the fact that, when the enteral feeding of vitamin B fails the parenteral administration may give an immediate cure, and it is difficult to avoid the conclusion that disturbance of intestinal function of very peculiar type plays an important part in the development of a shortage of vitamin B.

III. *A. Delay in Recovery from Beriberi. B. Inactivity of Parenteral Vitamin B.*—In this communication it is shown that sometimes the parenteral administration of artificial vitamin B is unsuccessful whereas the same vitamin B given by the mouth brings about cure. This leads the author to the conclusion that artificial vitamin is not a full vitamin that it is, indeed, vitaminogen or provitamin, which is convertible in the intestine into the active product, vitamin B. If this conversion does not take place, whether in the intestine or by subcutaneous injection, the state of avitaminosis will persist. The hitherto observed cases of delayed recovery from beriberi are in all probability enterogenic forms of beriberi in the sense of SCHÜFFNER. *W. F. Harvey.*

SOETJAHJO & GAN SING BIE. Over de werking van het antineuritische vitamine (B) van de I. G. Farbenindustrie A. G. bij een geval van beri-beri. [**On the Action of the Anti-neuritic Vitamin B in a Case of Beriberi.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. July 17. Vol. 74. No. 15. pp. 951–954.

The adrenalin test of Aalsmeer has been made use of to gauge the value of the preparation of anti-neuritic vitamin used. If, moreover, a vitamin-poor diet first increases this effect of adrenalin and then the administration of vitamin B promptly causes it to diminish, it is considered legitimate to look on the test as a complete measure of the degree of beriberi affection.

The method of carrying out the test is as follows:—First of all the grade of beriberi is determined by application of the adrenalin test in conjunction with the pitressin test. Then the patient receives a vitamin-poor diet for 5 days. The adrenalin-pitressin test is next applied again. If now the symptoms appear changed for the worse, injections of the test vitamin are given (twice daily for 5 days), and the patient should then be enabled to remain on his vitamin-poor diet. The following case is illustrative:—"A patient with active beriberi, definite heart and vessel symptoms, pareses and oedema gave with rest in bed an increase in the minimal bruit-forming pressure and a slight increase of diuresis (but not more than 1,250 cc.)—an indication of relief of the strain upon the heart. When the vitamin-poor diet was begun there occurred first a lowering of the minimum bruit-pressure and then a rise, but it remained too low (40 mm.). The pulse remained still above 100, the oedema was unchanged and the pitressin effect remained negative after these 5 days of vitamin-poor diet, which is the testing indication that the beriberi had changed for the worse. The injections now given furnished the following result: (1) The diuresis was increased (2 litres) so that after the

injections were stopped the oedema diminished. (2) The pulse rate fell from over 100 to 76. (3) The minimal bruit-pressure increased from 40 to 60 mm. (4) The adrenalin reaction became negative. (5) Motor and sensory disturbances, although diminished, were still present . . . .

Thus it was shown that after subcutaneous injection recovery from the state of avitaminosis was rapid. The continued presence of neurological symptoms offers no contradiction, as they are no measure of the degree of deficiency in vitamin B (secondary degeneration). . . . It seems desirable therefore that the name anti-beriberi vitamin should be substituted for anti-neuritic vitamin." *W. F. Harvey.*

RIESMAN (David) & DAVIDSON (Harold S.). **Beriberi following Drastic Voluntary Dietary Restriction**—*Jl. Amer. Med. Assoc.* 1934. June 16. Vol. 102. No. 24. pp. 2000–2003. [11 refs.]

Two cases are described in which beriberi developed following the voluntary consumption of a deficient diet.

Particulars of the two cases are as follows :—

Case 1.—The patient, a white male aged 76, had for many years suffered from stomach trouble, with the result that he gradually eliminated different articles of food from his diet. About one and a half years before admission to hospital he was so ill that he gave up all food except milk, of which he took about three quarts a day. This caused diarrhoea, so that he was forced to reduce the milk intake by half. Progressive weakness set in, and his legs began to swell. On examination the man was found to be emaciated, pale and mentally confused. The hands, face and legs were oedematous, the calf muscles were extremely tender and the heart was enlarged to the right. The legs and buttocks also presented large ecchymotic spots. A diagnosis of beriberi was made. Two blood transfusions, of 250 cc. each on successive days, were given, and, through a stomach tube, large amounts of vitamin B extract, orange juice, beef juice, egg, tomato juice and cod liver oil were administered, together with adequate doses of iron and ammonium citrate. After a few days the patient removed the tube saying that he could feed himself. He then developed a ravenous appetite and began to consume a normal diet supplemented with vitamin B extract and iron. Within two weeks the oedema subsided, and a month later he was able to walk about feeling cheerful and better than he had done for years.

Case 2.—A young woman, much over weight, tried to reduce her adiposity by living upon a meagre and monotonous diet. After a few weeks dyspnoea, palpitation and oedema of the legs appeared. No primary cardiac trouble was found, and beriberi was diagnosed. The return to a sensible diet alone resulted in prompt recovery.

The authors describe other similar cases collected from the literature, and they are of the opinion that " as long as fashion decrees the sylphlike figure, sporadic cases of beriberi are likely to occur." *A. D. Bigland.*

VAN VEEN (A. G.). Over het nut van niet gewasschen, weinig geslepen rijst als dagelijksch voedsel. [**The Use of a Ration of Unwashed Slightly Polished Rice.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. May 22. Vol. 74. No. 11. pp. 672–680. Full German summary.

This is a continuation of work already summarized in the *Bulletin.* A series of experiments is described dealing with the vitamin B_1 loss

sustained in the preparation of much larger quantities of rice, such as are used in the army, prisons and large plantations.

It was again determined that washing of rice of whatever degree of milling is very detrimental to its vitamin content, as proved by experiments with birds. On the other hand, steaming is very much less harmful in this respect, and also has the advantage of saving water and labour. Local objection (in Java) to unpolished or slightly polished rice, is chiefly on account of its red colour and not its taste; hence it is recommended that " silverskin " rice or other pale varieties be used, and that the washing of the product be omitted as far as possible. It is found by experience in prisons, plantations, etc., in Java that the custom of adding large amounts of vegetables as accessories to a polished rice diet is not acceptable to the native taste, especially when the consumption of large amounts of cooking water is also insisted upon. *A. D. B.*

VAN VEEN (A. G.) & KOKS (M. T.) Over den invloed van het Claytoneeren op het B_1-vitamine-gehalte van rijst. [**The Effect of Clayton Disinfection on the B_1-Vitamin of Rice.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Apr. 10. Vol. 74. No. 8. pp. 482–485.

In order that the experiments might be as natural as possible the samples of rice were taken from the holds of ships which had been Claytonized. The B_1-content was expressed in International Standard Units. In the first trials sacks of about 2-kilogm. content were used and then sacks of larger size. Claytonization does affect the content of rice in vitamin B, and this reduction is greater the more polished and the moister the rice is. In sacks of some-kilogram size the B_1 vitamin of dry gabah rice is definitely diminished, that of dry silver-cuticle rice by more than one-third and that of half polished rice by about one-half. With larger sacks the effect is not so marked, due probably to non-penetration of the sulphur dioxide gas. Pure vitamin is practically not affected by a dilute solution of SO_2 at pH 3 to 7 and only slowly by concentrated solutions. The concentration of the B_1 vitamin in the samples used was estimated by trial upon rice birds. *W. F. Harvey.*

SHIN (Hitsuko). **Basic Studies on Beri-Beri in Pregnancy and the Puerperium and also in Early Infancy.**—*Trans. Soc. Path. Japon.* 1933. Vol. 23. pp. 295–306.

An account is given of experiments on rabbits showing the vitamin B content of the various organs under normal conditions and during pregnancy and the puerperium.

The vitamin content in the various organs of unmated rabbits was first studied. The liver and spleen give the highest figures, while progressively decreasing amounts were found in the kidney, lung and brain (equal), cardiac muscle, blood and voluntary muscles. The mammary glands contain none at all. During pregnancy the vitamin B content markedly decreases, especially in the liver, lung and brain. This is due not to excessive excretion from the kidney, where there is apparently an increased store, but to the increasing consumption of the vitamin by the growing embryo. An even greater fall in vitamin B content is found during the puerperium, but the kidney

still contains more than normal. The mammary glands during pregnancy and the puerperium contain an increased supply of vitamin. The above findings point to the liability of beriberi occurring in human subjects during this physiological state, especially if the vitamin B content of the diet is lessened.

A further series of experiments, this time using vitamin B-deficient diets, was carried out. It was found that feeding rabbits on such diets considerably reduced the vitamin B content of all organs and secretions, and the effect was especially marked during pregnancy and the puerperium. The liver was depleted more rapidly than the other organs. This is a most important finding since the liver is known to be a storage organ supplying vitamin B to the other tissues. It seems, therefore, that such diets during pregnancy and the puerperium must render the individual more than ordinarily liable to contract beriberi. On such vitamin B-deficient diets not only does the embryo suffer, but the vitamin content of the mother's mammary glands is decreased to one-fifth of that of a normally fed mother, and the suckling may easily contract beriberi. It was also found that such diets bring about important changes in the distribution of vitamin B throughout the body.

A third set of experiments showed that if the diet of the mother is lacking in vitamin B, even for a few days, the vitamin content of the embryo and of the mother is decreased. The same was found to be true of the mammary glands and the milk derived therefrom. Thus an infant may develop beriberi before the inadequately nourished mother shows any symptoms of the disease. *A. D. B.*

JOURNAL OF THE INDIAN MEDICAL ASSOCIATION. 1934. Sept. Vol. 4. No. 1. pp. 12–13. **Epidemic Dropsy.**

Calcutta is again experiencing an outbreak of epidemic dropsy, and the present paper is in the form of an editorial dealing with the subject in general.

Among the epidemiological data are the following :—

The Northern part of the city is the more affected as it was in the epidemics of 1926 and 1932. Previous epidemics have been recorded in 1877, 1878, 1901, 1909, 1919, 1926, 1927, 1930, 1931 and 1932. "The morbidity is highest amongst the Bengali Hindus, moderate amongst the Mahomedans and least amongst the Marwaris. Europeans escape altogether." Some observers hold that the disease is due to the ingestion of toxins produced in badly stored rice by some spore-bearing bacillus, but in some outbreaks (as in Fiji) damaged rice cannot be held responsible. The taking of mustard oil is regarded by others as an important etiological factor. The following reasons are given in favour of the view that the disease is probably not a primary intoxication but an infection :—

" (1) Seasonal incidence in July when long continued rains and humidity are present.
" (2) Widespread epidemicity.
" (3) Greater incidence amongst people living in riverside places, suggesting the possibility of a water-borne infection.
" (4) Occasional incidence of the disease amongst persons who come in contact with a patient of epidemic dropsy where dietetic and environmental factors have been definitely eliminated.

" (5) The frequent spread of the disease from towns to the villages.
" (6) Recurrent and chronic course of the disease as is shown by the persistence or re-appearance of oedema of the legs, of gastro-intestinal and cardiac disturbances."

It is suggested that further research should be directed towards the bacteriological study of the intestinal flora of sufferers together with immunity reactions against any suspected organism isolated. Attempts should also be made to reproduce the disease in suitable experimental animals. *A. D. B.*

PURCELL (F. M.). **Beri-Beri or Epidemic Dropsy.**—*West African Med. Jl.* 1934. Apr. Vol. 7. No. 4. pp. 143–145.

A case of general anasarca in an African child is described. A diagnosis of epidemic dropsy was made. The child had lived exclusively upon cassava, and details of the preparation of this tuber are given.

Beriberi is uncommon in the Gold Coast, only 16 cases being reported in 1930 and a smaller number in the following year. Rice is the staple food of the Kroos alone, but the disease apparently is not confined to this tribe. If vitamin deficiency were the sole cause of beriberi the disease should occur sometimes in epidemics since in any one tribe the staple food is constant. Such epidemics have not been observed in the Gold Coast, and it seems that none of the tribal diets is deficient in neuritis-preventing vitamin.

One case is described. The patient, an African child, was admitted to hospital having been sick for one week. He presented general anasarca, marked tachycardia with orthopnoea, enlarged heart with signs suggesting hydropericardium, mild fever and hepatic and splenic enlargement. The knee jerks were absent, but it is stated that subsequently no evidence of peripheral neuritis was discovered. The patient was successfully treated with heart tonics and magnesium sulphate. The author is of the opinion that this was a sporadic case of epidemic dropsy.

The child's diet consisted of cassava and apparently nothing else. In the Ada district the diet consists almost exclusively of this tuber, which is scraped and dried in the sun. While drying a black saprophytic fungus, rhizopus, grows upon it, and the natives think that this improves the food. Cassava is practically pure carbohydrate with very little protein and probably also deficient in vitamins. The physique of the Ada people is poor in consequence. *A. D. B.*

MASSIAS (Charles). Présence de bacillus mésentéricus dans une hémoculture au cours d'un épisode fébrile chez un ancien béribérique.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Feb. Vol. 12. No. 2. pp. 173–174.

MÉHES (J.). Die Wirkung der Digitalisglykoside bei an Beriberi erkrankten Tauben.—*Arch. f. Experim. Path. u. Pharm.* 1934. Aug. 30. Vol. 176. No. 2/3. pp. 141–159. With 2 figs. [14 refs.]

—— & PÉTER (F.). Die Wirkung des Digitoxins auf das Ekg der normalen und der an experimenteller Beriberi erkrankten Tauben.—*Arch. f. Experim. Path. u. Pharm.* 1934. Aug. 30. Vol. 176. No. 2/3. pp. 226–237. With 5 figs. [24 refs.]

SLEEPING SICKNESS.

DUKE (H. Lyndhurst). **On the Protective Action of "Bayer 205" against the Trypanosomes of Man.**—*Lancet.* 1934. June 23. pp. 1336–1338.

Details are given of a number of experiments devised with the object of ascertaining how long Bayer 205 would protect man against infection with *T. rhodesiense* and *T. gambiense.*

In his introductory remarks, Duke states that although prevention is better than cure, prophylaxis against the diseases of man by the use of drugs could claim little or no success before the appearance of "Bayer 205." For many years the medical profession has been debating about the value of quinine as a prophylactic in malaria. The work of the reviewer and MACFIE (1924) was, however, the first scientific warning that all might not be well with the time-honoured ritual, practised the world over by Europeans "east of Suez," of the 5-grain tablet taken each evening with the first "sundowner." A commission of the League of Nations has studied the question experimentally, and in the third general report of the Malaria Commission the conclusion is promulgated that "No drug which is known, taken in harmless doses, can be guaranteed to act as a true causal prophylactic."

A summary is given of the earlier observations of the prophylactic action of "Bayer 205" against infection in animals and man with various trypanosomes. Although the general inference to be drawn from this work is that "Bayer 205" has a definite prophylactic value, nevertheless the evidence so far accumulated is not entirely conclusive.

The author's experiments were commenced in connexion with an investigation on the effect of long residence in antelope of the trypanosomes of man. Volunteers were used for this work and those who became infected were treated with "Bayer 205" the moment trypanosomes were demonstrated in their peripheral blood. Three of these cases (A, B and C) were chosen as the starting point of the present research. Each of these men was infected with a strain of *T. rhodesiense* which had been for months in an antelope at the laboratory. All three became infected after an incubation period of 8 to 10 days, and each was treated with a series of 6 doses of 1 gm. of "Bayer 205," the doses being given at an interval of a few days.

At the Conference on Trypanosomiasis held last November at Entebbe, the examination of the prophylactic value of "Bayer 205" was allocated to the Uganda Institute. Three healthy native volunteers (cases I, M and Q) were selected, and each was given a single intravenous injection of 1 gm. of "Bayer 205"; and another treated volunteer (E) was added to the first list. In addition, 3 monkeys were also given a prophylactic dose of the drug varying from 0·158 gm. to 0·023 gm. per kilo.

At various intervals, after the administration of the drug, the volunteers and the monkeys were subjected to the bites of tsetse flies infected with different strains of *T. rhodesiense* and *T. gambiense*, respectively. Details are given in the table, which is reproduced (p. 9).

Those volunteers (A, B, C and E) who had been treated with 6 doses of "Bayer," after being infected for some 10 or 11 days with *T. rhodesiense*, resisted all attempts at re-infection with different strains of *T. rhodesiense* for at least 190 days. On the other hand, the

Table showing the exposure of volunteers previously inoculated with Bayer 205 to cyclical infection with human trypanosomes carried by G. palpalis.

Days after last inoculation of Bayer 205	Volunteers							Monkeys			Days after last inoculation of Bayer 205	Volunteers						
	A	B	C	E	I	M	Q	1226†	1227†	1229†		A	B	C	E	I	M	Q
38	...	...	2g	...	...	...	...	...	...	...	103	...		...	1d	...	$5b^3$	...
39	3a	...	...	...	...	...	...	...	...	...	104	...		...	...	...	$1b^3$	...
40	2a	...	...	...	...	...	...	...	...	...	105	...		...	$2b^2$	...	$2b^3$	...
63	1b	...	...	...	...	...	$1b^2$	...	...	...	107	...		...	...	...	...	$6b^3$
66	...	...	...	...	...	...	$1b^2$	...	...	...	108	...		...	...	$1b^3$	...	$1b^3$
67	...	...	...	...	...	$1b^2$	...	$1b^2$	...	...	110	...		...	...	$3b^3$	...	...
68	...	...	...	...	...	1c	...	$1b^2$	...	...	111	...		...	...	$4b^3$	...	...
69	...	...	...	...	...	...	...	...	$1b^2$	...	113	...		...	...	...	1e	...
70	...	...	...	...	1c	...	...	...	$1b^2$	...	133	...	$1b^2$	...	...	...	...	...
72	...	...	...	...	1c	...	...	...	...	...	134	...	...	$1b^2$	...	...	...	...
74	...	...	...	...	...	1c	1c	...	...	1d	136	...	$1b^2$	...	...	...	...	...
75	...	...	...	...	...	1d	1d	...	...	...	142	...	...	$2b^2$	...	...	...	...
76	...	...	...	...	...	$2b^2$	$2b^2$	...	...	...	145	...	...	$2b^2$	...	...	$**1g^2$	...
						1d	1d				146	1c	...	...	...	...	...	...
77	...	...	...	...	...	$2b^2$	$2b^2$	...	...	1d								
						1d	1d				147	...	$1b^3$	...	...	...	...	...
78	...	...	...	...	...	$1b^2$	$1b^2$	...	...	...				...	...			
79	...	...	...	...	...	1d	1d	...	...	...	149	1d	...	...	...	...	...	...
80	...	...	...	...	$2b^2$	...	...	...	...	...	174	...	...	$2b^3$	...	...	...	...
81	...	...	...	...	$2b^2$	...	...	...	...	...	179	...	$1b^3$	$4b^3$	...	...	...	...
82	...	...	...	...	1d	...	...	...	...	...	180	...	$1b^3$	$1b^3$	...	...	...	...
83	...	...	...	...	1d	...	...	...	...	...	181	...	...	$1b^3$	...	...	...	...
88	...	...	...	...	...	...	...	...	...	...	182	...	...	$2b^3$	...	...	...	...
91	...	...	$1b^1$	...	...	...	...	...	...	...	187	1e	...	...	...	...	...	...
92	...	...	$3b^1$	...	...	...	...	...	...	...	190	2e	...	...	...	...	...	...
95	...	...	$2b^1$	$1b^2$	...	...	...	...	...	...	208	...	$2g^2$	...	...	...	...	...
99	...	...	...	...	...	...	$2b^3$	...	...	...	210	...	$4g^2$	...	...	...	...	...
100	...	$1b^1$	...	...	...	...	...	...	...	...	212	...	$1g^2$	...	...	...	...	...

EXPLANATION.

The numerals in the columns show the number of gland-infected flies biting man on that date.

a = *T. rhodesiense* strain Tinde III (passage 1) controls : volunteers N and O, both infected.
b^1 = " " LX (" 1) control : " T infected.
b^2 = " " " (" 2) " " V "
b^3 = " " " (" 3) " " D "

c = *T. rhodesiense* strain Tinde II control : volunteers U infected.
d = " " " III (passage 2) " " X "
e = " " " " (" 3) " " ** "
g = *T. gambiense* " LX.1 " " P "

g^2 = *T. gambiense* strain LXII (*cf.* text).

** This fly was dissected the day after it fed on Volunteer M. Both salivary glands were heavily infected and the alimentary canal was full of M's blood.

† Trypanosomes appeared in 1226's, 1227's and 1229's blood 11, 9 and 8 days respectively after the first fly bite.

monkeys were found to be sensitive to infection with *T. rhodesiense* 67, 69 and 74 days respectively after treatment with a single dose of "Bayer." It is to be noted that each of these animals proved to be sensitive the first time it was examined.

Duke states that the results obtained with *T. gambiense* are particularly instructive. Volunteer M was bitten on the 113th day by a fly infected with *T. rhodesiense*, but he did not become infected. On the 145th day he was bitten by 2 flies infected with *T. gambiense* and 9 days later was found to be infected. From this, Duke concludes "The administration of a single dose of 'Bayer 205' had therefore protected this man against *T. rhodesiense* for at least 113 days, but by the 145th day he was no longer safe against *T. gambiense*." Turning to the 6-dose series of volunteers, it is seen that B was bitten by 7 flies infected with *T. gambiense* between the 208th and 212th days after the last dose of "Bayer"; 22 days later he was found to be infected. It thus appears that volunteer B, who was protected against *T. rhodesiense* for at least 180 days after the last administration of "Bayer 205," possesses no defence against *T. gambiense* on the 208th day. It has not yet been determined how long protection lasts against *T. gambiense* in man; the only other experiment performed with this trypanosome being that of volunteer C who resisted infection 38 days after his last dose of "Bayer 205."

In his conclusions Duke states that it is probable, though not yet proved, that the protection conferred by "Bayer 205" is greater against *T. rhodesiense* than against *T. gambiense*. He adds that at the present time, to be on the safe side, he considers that the prophylactic injection of 1 to 1·5 gm. of "Bayer 205" per adult should be repeated every 3 months while exposure to infection continues. He further considers that the natural sensitiveness of the mammal to the trypanosomes plays an important part in determining the duration of the protection conferred by "Bayer 205," the more susceptible monkey receiving less protection per dose per kilo. of body weight than the more resistant man. *W. Yorke.*

DUKE (H. Lyndhurst). **On the Employment of Volunteers in Trypanosomiasis Research; and on the Element of Control in Experiments with Trypanosomes and Glossinae.**—*Parasitology*. 1934. Aug. Vol. 26. No. 3. pp. 315–324.

Two subjects are dealt with in this paper which, in the author's opinion, are of practical importance to those interested in research on trypanosomiasis; these are the employment of volunteers and the necessity for control in experiments on Glossina.

In discussions on the zoological status of *T. gambiense*, *T. brucei*, and *T. rhodesiense*, it is generally assumed that *T. brucei* cannot infect man, whereas the other two can. The true affinities of all these trypanosomes can, however, be revealed only by direct experiments on man himself, and until the last year or so the risks connected with such experiments precluded their employment on anything like an adequate scale. Recent advances in chemotherapy have removed the main obstacle to experiments on man, and it is now safe to use volunteers. CORSON was the first to test on himself a trypanosome known to have been at one time pathogenic to man [this *Bulletin*, Vol. 29, p. 634], and shortly afterwards FAIRBAIRN performed a similar experiment on himself.

The employment of native African volunteers began with certain investigations carried out at Entebbe two years ago. Duke states that

he thinks all will agree that it is in practice impossible to settle the unsolved problems of trypanosomiasis without the assistance of native Africans : the number required alone justifies this contention. Up to the present, in the investigations in Uganda into the antelope reservoir and the prophylactic results of " Bayer 205," 24 native volunteers have been employed. All these men fully understood the significance of their contract. So far 16 of them have become infected and there has been no untoward event in the subsequent career of any. The regular method of infection employed is the bite of a cyclically infected fly, or, in rare instances where this is impossible, the subcutaneous inoculation of its glands. In addition to the more obvious points to be considered with the use of volunteers, there is the theory recently advanced by CORSON that there may be a state of cryptic trypanosomiasis set up in man by strains of *T. rhodesiense* which have been exposed for long periods to the tissues of resistant animals such as antelope [this *Bulletin*, Vol. 29, p. 634]. After considering this matter in some detail, Duke comes to the conclusion that it is very unlikely that this hypothetical cryptic infection with *T. rhodesiense* ever occurs in man.

Dealing with the second subject, Duke states that in any prolonged investigation on African mammalian trypanosomes, especially where Glossina are used as agents of infection and ruminants as the vertebrate host, it is of the first importance to establish an efficient system of control against accidental infection with trypanosomes other than those which it is intended to investigate. During the last year or two the main subject of research at Entebbe has been the study of game animals, especially antelope, as a reservoir of the trypanosomes of man, and in such an inquiry supreme importance attaches to the question whether a given trypanosome is or is not pathogenic to man. To carry out this research clean antelope were collected at the Institute and some of them were set aside as controls. Some months ago, one of the control animals was found to be infected with a trypanosome indistinguishable from the *T. rhodesiense* carried by its experimentally infected companions.

In the antelope enclosure there lived freely together three adult bushbuck, 4 oribi, one adult and 2 young situtunga, 4 reedbuck, and a ntalaganya. Of these, one of the situtunga, a ntalaganya and a reedbuck were kept as controls. After some time it was discovered that the control reedbuck was infected.

Duke examines in great detail the possible ways in which this untoward event had occurred. For reasons given he is able to exclude the possibility of the control reedbuck being infected when it reached the laboratory, and similarly he excludes the possibility that the animal was infected with wild *Glossina palpalis* as he is satisfied that these flies never succeed in reaching the present laboratory. The explanation of the phenomenon seems to be the direct transmission of the trypanosomes ruminant to ruminant by Stomoxys. The three young reedbuck were observed to keep close together all through the day, thus facilitating the direct transference of trypanosomes from one to the other. Moreover, trypanosomes were common in their peripheral blood. Stomoxys were numerous in the animal enclosure and dissection of several hundreds caught in the antelope's stable revealed in the partially digested blood of the hind-gut of a single fly a few feebly-moving trypanosomes which had presumably been taken up from one of the antelope. *W. Y.*

British East African Territories, Conference of Governors of: **Research Conferences. Conference on Tsetse and Trypanosomiasis (Animal and Human) Research. Held at Entebbe, 22nd to 25th November, 1933.**—42 pp. 1934. Nairobi: Govt. Printer.

The Governor of Uganda in opening the Conference stated that this was the first of what he hoped will prove an exceedingly valuable series of conferences. The co-ordination of scientific research in East Africa is one of the duties which has been specially assigned to the Governors' Conference, and when they discussed the question last February they reached the unanimous conclusion that at the moment co-operation and co-ordination were not as complete as they might be. With the object of remedying this they had decided to call together representatives of the various East African Colonies of Kenya, Nyasaland, Tanganyika and Uganda. He also welcomed Dr. Fontana, Chief of the Medical Service of the Province Orientale of the Belgian Congo.

The Agenda is divided into three sections :—

A. Items from the programme of Research suggested by the Second International Conference on sleeping sickness [this *Bulletin*, Vol. 26, p. 185]. These include—the question of natural immunity, spontaneous cure and acquired immunity of man, and natural immunity of the baboon and its relationship with serum-resistance ; other reservoirs of *T. gambiense* than man and new means of diagnosis ; the origin of *T. rhodesiense* and its relationship to *T. gambiense* and *T. brucei* ; the transmission of acquired characters through Glossina ; the evolution of the polymorphic trypanosomes in tsetse and the factors which influence it ; pathological investigations in infected animals ; biological studies of tsetses ; the factor determining the infectivity of trypanosomes for tsetse ; therapeutic researches, etc.

B. Items of research suggested by investigators in the East African Territories, *e.g.*, bionomics of *T. uniforme* and *T. brucei* ; cultivation of trypanosomes ; the control of trypanosomiasis in man and animals by chemotherapy, by administrative methods, and by control of tsetse ; diagnostic methods in trypanosomiasis ; mechanical transmission of trypanosomes by vectors other than tsetse ; the pathogenicity of various trypanosomes for different animals, etc.

C. The future of trypanosomiasis and tsetse fly research in East Africa.

At the general discussion which took place on the agenda, it was decided to arrange the program of research first, leaving the question of the future of trypanosomiasis and tsetse-fly research in East Africa to be dealt with later.

After much discussion a program of tsetse and trypanosomiasis research was agreed upon ; this program is summarized in the table (p. 13).

The Conference then proceeded to the discussion of the future of trypanosomiasis and tsetse research in East Africa. After Duke had outlined the position in regard to protozoological research and the financial difficulties of the Human Trypanosomiasis Institute, the Conference considered the advisability of preserving a Central Research Institute, and the opinion was expressed that the present was not a time at which a definite pronouncement on such a subject could be made. It was felt that, whether or no a Central Institute

could be established, other laboratories where local problems in connexion with trypanosomiasis could be investigated would still be essential. Finally the Conference :—

" (1) considered that the present time was inopportune to give an opinion as to whether the Human Trypanosomiasis Institute should be continued as a permanency ;

" (2) recommended that, if the Government of the Uganda Protectorate agreed, this Institute should be kept on for another year on its present footing and that the question should then be reconsidered ;

" (3) having discussed the programmes of research in hand in the various laboratories and in the field, recorded its opinion that no overlapping of research was taking place in East Africa other than that which was necessary for the establishment of essential facts."

Summary of Program of Tsetse and Trypanosomiasis Research.

a = Human Trypanosomiasis Institute, Entebbe.
b = Veterinary Laboratory, Entebbe.
c = Veterinary Laboratory, Mpwapwa.
d = Trypanosoma Rhodesiense Laboratory, Tinde.
e = Medical Laboratory, Nairobi.
f = Medical Laboratory, Nyasaland

Item of Research	Where to be carried out
(*a*) Question of natural immunity, spontaneous cure and acquired immunity in man ...	a, c and d.
(*b*) Experiments on relatively resistant ruminants with strains of *T. rhodesiense* and *T. gambiense* obtained over as wide an area as possible ...	a, c and d.
(*c*) Existence of other reservoirs of *T. gambiense* than man	a.
(*d*) Retention of acquired characteristics by trypanosomes during cyclic evolution in body of tsetse	a (*T. gambiense*). c (*T. congolense* and *T. vivax*). d (*T. rhodesiense*).
(*e*) Evolution of different trypanosomes in body of tsetse and other biting flies and relationship to environment (climate, etc.) of cyclic transmissibility and pathogenicity	a, b, c and f.
(*f*) Biological studies of tsetse-flies in *T. rhodesiense*, *T. gambiense* and *T. brucei* areas	Work now being carried on in various territories to be continued.
(*g*) Study of food supply of tsetse as determined by biological study of stomach contents of fly ...	e.*
(*h*) Investigation of the prophylactic value of Bayer 205	*a*.†
(*i*) Further investigation of identity of *T. uniforme*	a and b.‡
(*j*) Investigation of bionomics of *T. brucei* ...	b.
(*k*) Cultivation of *T. congolense* and *T. vivax* on artificial media	b.
(*l*) Control of tsetse-fly	Work now in hand or projected in all territories to be continued or put in hand.
(*m*) Trypanosomiasis of pigs	b and c.§

* Mr. Swynnerton prepared to assist in supply of sera from game animals when opportunity offered.

† A large-scale field experiment to be conducted in Tanganyika should the laboratory experiments indicate the necessity therefor.

‡ Every endeavour to be made to furnish a strain to Mr. Hornby.

§ Material acquired in any territory to be transmitted to either of these laboratories.

SWYNNERTON then explained the present position and the amount of collaboration which was already in existence as regards tsetse-fly research in East Africa. The Conference after some discussion :—

" (1) recorded its appreciation of the great practical importance of the work of the Tanganyika Tsetse Research Department to all three territories as regards the control of both animal and human trypanosomiasis (*vide* Appendix III) ;

" (2) recorded its conviction of the need, not only for this work, but also for every facility being given by the respective Governments to continue and extend the present opportunity for personal co-operation and collaboration without regard to inter-territorial boundaries."

A discussion took place on the facilities which existed for the communication of results of the trypanosomiasis research which is being carried on in the various laboratories in the Colonial Empire. DUKE and CORSON informed the Conference of the very valuable help they had received from the " Tropical Diseases Bureau." The Conference, after discussion :—

" (1) recorded its opinion that further facilities for the distribution of published and unpublished reports should be given, and recommended that some central body in England should be approached with a view to its undertaking the distribution of reprints, etc., to workers who might be interested ;

" (2) recognized that this would involve the provision of a greater number of reprints, and recommended that the cost of such should be borne by the Government concerned."

The report closes with a memorandum by MACLEAN on the control of trypanosomiasis in man and animals by chemotherapy and administrative measures ; and with a memorandum by SWYNNERTON giving an account of the work which had been carried out in East Africa either by the Tsetse Research Department in Tanganyika or by members of the Medical and Veterinary Departments in other territories in collaboration. *W. Y.*

LEDENTU (G.). La lutte contre la maladie du sommeil au Cameroun. [**Campaign against Sleeping Sickness in Cameroon.**]—*Ann. Inst. Pasteur.* 1934. Aug. Vol. 53. No. 2. pp. 174–220. With 8 diagrams.

This paper describes the work of the sleeping sickness organization in Cameroons since 1930. In a recent paper JAMOT has summarized the work of the mission between 1924 and 1930 [this *Bulletin*, Vol. 29, p. 633].

In 1931 the sleeping sickness prophylaxis service was dissolved and the whole organization changed, owing to the acute economic crisis. From 36 European officers and 400 native assistants it became necessary to reduce the service to a minimum compatible with safety. The new organization, which still remained centred in Ayos, the main epidemic focus, consisted of 5 teams for diagnosis, each composed of a doctor and 20 assistants, and more than a dozen teams for treatment, each composed of a European sanitary officer and 3 hospital attendants. The general organization which had proved so satisfactory in the past was thus maintained but modified so as to meet the financial needs of the time. In 1934 it was found possible to reinforce the service to some extent.

The very lengthy report which follows takes the same general form as that of JAMOT, 1932. A detailed account is given of the progress of the disease in the various subdivisions of the epidemic zones, in which the initial morbidity was everywhere over 15 per cent. ; in the endemo-epidemic zones, in which the infection rate was in some places over and in other places less than 15 per cent. ; and finally in the endemic zones, in which the infection was everywhere less than 15 per cent. [Those interested must consult this part of the paper in the original.]

The general impressions produced by this summary appear to be :—

1. In the zones of feeble endemicity the disease has nowhere gained ground and in places it has definitely retrogressed.

2. In the endemo-epidemic zones the results have been considerable. The vast focus in the north constituted by the subdivisions of Doumé and Nanga-Eboko has been reduced to one of feeble endemicity. The two western foci of Manguissas and Etons appear to be extinct ; that of Bafia is reduced to the Yambassa tribe, but here it offers a stubborn resistance. The southern focus of Sangmélima has almost disappeared.

3. In the epidemic zones the focus of Bertoua is extinct, as is almost that of Batouri. The same cannot be said, however, of the foci of Haut Nyong and of the upper reaches of the Dja ; and there is some revival of activity among the Omengs, the Makas and the Yébékolos of Akonolinga.

The broad facts emerging from this survey are that the disease has undergone rapid retrogression, sometimes spontaneously, in most of the peripheral zones of extension, but that there is some recrudescence in the old foci. In the old foci of Nyong and of Dja the infection is proving resistant and in certain places is even increasing, but the index of peripheral infection is, however, not comparable with that observed in 1926–1928, when it was 35 to 45 per cent. To-day such a figure as 5 per cent. is exceptional.

It is difficult to understand why trypanosomiasis in certain zones readily yields to treatment, whilst in others it is resistant to the same treatment. Differences of race, of habitat, of abundance of Glossina, and of virulence of the pathogenic agent undoubtedly play a part, but these factors are not the whole explanation. The drugs seem to have lost their power to sterilize rapidly the blood of carriers in certain districts, and lumbar puncture of 5-year-old cases in apparently excellent health shows that about a quarter of them exhibit meningeal changes. [It is possible that the difficulty in sterilizing the infected in the old foci of the disease may be due to the fact that prolonged treatment of the disease in these areas has resulted in the production of " arsenic fast " strains of trypanosomes which are now being propagated by Glossina.] *W. Y.*

BERTRAND (Yves). Résultats de 601 ponctions lombaires effectuées dans une région à maladie du sommeil (Nord-Togo). [**Results of 601 Lumbar Punctures in a Sleeping Sickness District.**]—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 522–526.

The paper is an analysis of the results provided by 601 lumbar punctures in the Lassa canton of the Pagouda sleeping sickness sector of North Togoland.

The total population examined was 11,023 and of these 5·3 per cent. had trypanosomes in the glands or blood. Lumbar punctures were made in 601 cases : of these 364 were new patients with parasites in

the blood or glands, but not somnolent ; 26 were new cases with parasites in the blood or glands, and somnolent ; 120 were old cases 4 years under treatment and in good condition ; and 91 were suspected cases of sleeping sickness but with negative blood and glands.

The cerebrospinal fluid was examined in respect of :—(1) cytology, (2) protein content, and (3) the colloidal benzoin reaction. The results of these examinations in each of the 4 classes of case mentioned above are given in detail, and certain deductions are drawn.

The author considers that systematic lumbar puncture practised in the bush, in conjunction with blood and gland juice examination, constitutes the only scientific method of ascertaining the nature of the virus afflicting the country. It was found that amongst new patients of healthy appearance evidence of nervous lesion existed in no less than 34 per cent. Among the old patients treated 4 years previously and in apparently excellent health 24 per cent. exhibited evidence of meningeal lesions ; as did also 14 per cent. of the suspected cases. As a general rule the positive colloidal benzoin reaction seems to appear before the meningeal reactions ; it accompanies these reactions and is the more definite as the reactions are the more intense, and it tends to persist for some time after the reactions have disappeared. *W. Y.*

VAN DEN BRANDEN (F.). Contribution à l'étude de la transmission héréditaire du *Trypanosoma gambiense* chez l'homme. [**The Question of Hereditary Transmission of** *T. gambiense* **in Man.**]—*Ann. Soc. Belge de Méd. Trop.* 1934. June 30. Vol. 14. No. 2. pp. 199–201.

After briefly summarizing the scanty literature relating to this subject, the author mentions an instance in which hereditary transmission did not occur although all the conditions appeared to be very favourable.

A woman from Bumba was admitted to the hospital at Leopoldville in an advanced state of pregnancy. The peripheral blood contained numerous trypanosomes and the spinal fluid showed great excess of lymphocytes and of protein. She was delivered of a normal child two days after admission. Examinations of the infant's blood made on several occasions failed to reveal the presence of trypanosomes.

W. Y.

ELLIS (M.). **A Report on the Effect of Tryparsamide on Sleeping Sickness Cases.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 207–208.

The author has examined the effect of a course of tryparsamide on the peripheral infection in a large number of cases of sleeping sickness in Northern Nigeria.

The work was carried on in the Kirikasamma district of the Hadeija Emirate, Northern Nigeria ; it was undertaken in conjunction with Government mass survey and treatment. The positive cases (glands or blood) found during this survey were treated with a course of tryparsamide consisting for adults of 13 injections at 5-day intervals, the first dose being 1 gm. and the subsequent dose 2 gm. each. On the morning of the last injection all the cases under treatment were re-examined in exactly the same way as in the original survey. The results can be summarized as follows :—

Findings at the initial survey :—

Gland juice positive	717
Blood positive	112
Total	829

Findings after 12 injections (23 gm.) of tryparsamide :—

(*a*) Cases with glandular enlargement :—

Puncturable	239
Too small for puncture ...	212
Total	451

Cases with no glandular enlargement 378.

(*b*) Positive findings of trypanosomes :—

Gland juice	2
Blood	13
Total	15 = 1·81 per cent.

It is recorded that of these 15 positive cases 14 were originally diagnosed by gland juice examination and one by blood examination. After the course of treatment, 7 of these 15 cases exhibited glands large enough for puncture, whilst in 8 the glands were too small for puncture.

The conclusions are as follows :—

" 1. In this series of cases, 1·81 per cent. were resistant to tryparsamide.

" 2. In a majority of cases, tryparsamide causes a subsidence of the swelling of the posterior cervical glands.

" 3. The disappearance or the persistence of the glandular swelling is no criterion of cure by tryparsamide.

" 4. Tryparsamide is very lethal to trypanosomes in gland-juice, only two out of 717 cases still showing them after treatment."

W. Y.

Bonnet (M.). Sur l'efficacité de la tryparsamide chez les trypanosomés en 2e période. [**The Efficacy of Tryparsamide in the 2nd Stage of Sleeping Sickness.**]—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 659–663.

This note is a criticism of a recent paper by Loré and Marty, who express the opinion that those cases of sleeping sickness which have been treated with tryparsamide when in the first stage of the disease are found to be resistant to this drug when they have passed into the second stage [this *Bulletin*, Vol. 31, p. 202].

Doubtless in a region where trypanosomiasis has been treated in as intensive a manner as in the Cameroons, a certain degree of resistance of the virus to the trypanocidal action of drugs will be observable after some years ; but it will be an arsenic-resistance, and consequently a resistance to atoxyl and other arsenicals as well as to tryparsamide. It is, however, difficult to test the point in the second stage cases, because tryparsamide alone is active, and is used, in such patients.

Moreover, Bonnet argues that the observations published by Loré and Marty do not provide proof that the cases were actually tryparsamide resistant. The two groups of cases are not comparable.

Group A consists of a residue of old cases sent to Ayos because previous treatment had failed, whereas Group B consisted of freshly discovered cases which had not previously had tryparsamide or any other form of arsenical treatment. This fact seems sufficient in Bonnet's opinion to explain the great mortality observed in the first group. Then there is nothing to prove that the patients of Group A were first stage cases when they were first discovered. Furthermore, many of the Group A patients did not receive tryparsamide for a long time after their discovery. Of the 10 cases 8 were diagnosed between 1923 and 1926, and it is known that in the Cameroons tryparsamide came into general use only in May, 1927. Before this date they were treated with atoxyl or novarsenobenzol and they had progressed into the second stage.

In short, the only thing certain about the patients of Group A is that they had been given tryparsamide before they were lumbar punctured; it is absolutely impossible to state whether they were in the 1st or 2nd stage when tryparsamide was given, and consequently it is impossible to assume an acquired resistance to tryparsamide.

Bonnet then proceeds to give illustrations from his own experience and from that of others, which, in his opinion, prove that it is not a resistance to tryparsamide, acquired as the result of using this drug in the first stage, which explains the therapeutic failures obtained in certain cases. He re-examined the protocols of 156 sleeping sickness patients who died at Ayos in 1932. Of these 94 were old cases corresponding to Group A of Loré and Marty and 62 were second stage patients who had never previously been treated (Group B). The fact that 40 per cent. of these fatal cases belonged to Group B showed that the therapeutic failure was not due to tryparsamide resistance.

Bonnet does not entirely agree with Loré and Marty when they write that tryparsamide should never be used in first stage cases, as some of these, which cannot be successfully treated by atoxyl or orsanine, yield to tryparsamide; nevertheless in the majority of cases tryparsamide should be reserved for the nervous period. *W. Y.*

i. Millous (M.) & Maury (M.). Sur le traitement de la trypanosomiase au Cameroun par la tryparsamide. [**The Treatment of Trypanosomiasis in Cameroons by Tryparsamide.**]—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. p. 665.

ii. Marty (M.). Sur le traitement par la tryparsamide des trypanosomés en 2e période. [**The Treatment of Second Stage Trypanosomiasis by Tryparsamide.**]—*Ibid.* pp. 663–664.

i. In commenting on the paper of Loré and Marty [this *Bulletin*, Vol. 31, p. 202], Millous and Maury state that arsenic resistance appears to be a general phenomenon due to a too cautious use of insufficient doses of trivalent or pentavalent arsenicals owing to the fear of producing ocular accidents. They quote the reviewer as stating that "salvarsan-resistance or atoxyl-resistance implies tryparsamide resistance," but apart from this they consider the statements of Loré and Marty are open to other objections. There seems no evidence that Group A cases were in the first stage at the first time of treatment with tryparsamide. In reality they were a collection of patients who were given tryparsamide before they were punctured, which is, of course, quite a different thing.

ii. Marty replies to the above criticisms. He does not admit that he and Loré were in error when they classified their Group A patients

as being first stage cases. The original treatment they were given—1 dose of atoxyl and 12 doses of tryparsamide—was at that time the standard treatment for sterilizing the infection and not for nervous cases. The clinical records contain nothing suggesting that the patients had passed into the second stage of the disease. He adheres to the conclusion of Loré and himself that it was the administration of tryparsamide before the appearance of meningeal lesions which was responsible for the special resistance exhibited later. *W. Y.*

Lieurade (L.). L'urotropine intraveineuse associée aux arsenicaux dans le traitement de quelques cas de trypanosomiase en 2e et 3e périodes. [**Urotropine Intravenously associated with Arsenicals in the Treatment of 2nd and 3rd Stage Sleeping Sickness.**]—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 438–443.

Details are given concerning 12 advanced cases of sleeping sickness treated by urotropine and tryparsamide.

The urotropine was given intravenously in doses of 2 to 3 cgm. per kilo. at weekly intervals about 3 hours before the arsenical. Albuminuria and an increase of protein in the cerebrospinal fluid was almost always observed on the following days, but, as a rule, disappeared before the next dose was due. The results obtained were satisfactory in 6 cases, but unsatisfactory in the remainder. The author remarks [and with justice] that it might be argued that the good results were due to the tryparsamide alone : he, however, is of opinion that the association of urotropine with tryparsamide had accelerated and accentuated the beneficial results. *W. Y.*

Raingeard. Traitement par l'hyposulfite de soude des troubles oculaires dus aux trypanocides. [**Sodium Hyposulphite in the Treatment of Ocular Troubles due to Trypanocides.**]—*Rev. Mèd. et Hyg. Trop.* 1934. May–June. Vol. 26. No. 3. pp. 143–153.

An interesting, and possibly important, paper in which the author records the beneficial results he has obtained by the use of sodium hyposulphite in cases of trypanosomiasis treated with atoxyl or tryparsamide, who developed ocular troubles.

Details of the treatment of 26 such cases are given and the results are summarized in the table here reproduced.

It thus appears that in this series of 26 cases there were no less than 77 per cent. of successes, and in the 12 blind cases treatment was successful in no less than 9 cases. The successful results were not limited to recent cases, but were obtained also among those who had been blind or semiblind since 1928 to 1930.

Discussing the best dosage, the author points out that his results were most favourable in the group of cases which were given 15 injections on alternate days, each of 10 cc. of a 20 per cent. solution intravenously. It is emphasized that all these cases, with a single exception, were given tryparsamide treatment only after the course of hyposulphite, and consequently there is no doubt that it was the latter drug which caused the ocular improvement. The author points out that he did not examine the eyes with the ophthalmoscope as his work was carried out in the bush, but he emphasizes the essential fact that these people who had not been able to see for periods varying for from 2 to

Series.	Name	Age	First appearance of accidents		Treatment used		Sight very poor.	Almost Blind.	Blind.	Improvement.	Great improvement.	Recovery.	Success.	Failure.
			Old cases	New 1933	Ato-xyl	Tryp								
I	Elindi ...	55		+		+			+		++		+	
	Noumbi ...	38	+32		+			+			+++		+++	
	Liniebe ...	33	+30		+		+				+++		+++	
	Totole	35	+30		+			+		+			+++	
II	Mangoumbo ...	26	+20		+				+					+
	Matende ...	33	+31			+			+			+	+	
	Kanga ...	34	+29		+		+			+			++	
	Mipoudi ...	38	+29		+				+			+	+++	
	Doumba ...	32	+31		+				+			+	+++	
	Badondo ...	40	+28		+				+					+
	Mwele ...	35	+28		+				+	+			+	
	Bombo... ...	30	+28		+			+						+
	Boudzanga ...	36	+32		+				+	+			+	
III	Awe	35	+32			+		+				+	+	
	Dimeka ...	34	+31			+		+				+	+	
	Lele	35	+32			+			+			+	+	
	Manzamba ...	38		+		+	+					+	+	
	Alama	28	+31			+			+	+			+	
	Bangwa ...	32		+	+			+						+
	N'Danga ...	36		+	+				+					+
IV	Souangala ...	32		+	+		+		+			+	+	
	Mangoumba ...	35		+	+							+	+	
	Daminene ...	58		+	+		+				+		+	
	N'Koho ...	25		+	+		+							+
	Nanha ...	32		+		+	+					+	+	
	Maniebe ...	32		+		+	+					+	+	
	26		16	10	17	9	8	6	12	5	4	11	20	6

Percentage of cured ... ... 76·84 per cent.
,, uncured ... ... 23·07 ,,

even 5 years recovered within a few weeks a degree of vision which enabled them to get about and attend to their needs. [As the author himself freely admits, this work should be repeated on a sufficiently large scale.] *W. Y.*

Lassablière (P.) & Peycelon (A.). Action de l'iodo-bismuthate de quinine sur le *Trypanosoma gambiense*. [**Action of Quinine Iodo-Bismuthate on** *T. gambiense*.]—*Rev. Méd. et Hyg. Trop.* 1934. May–June. Vol. 26. No. 3. pp. 129–137.

A considerable number of guineapigs infected with a strain of *T. gambiense* were treated with quinine iodo-bismuthate.

A soluble and an insoluble form of the compound were used; the former was injected intramuscularly and also subcutaneously, the latter only subcutaneously. The results which are given in detail are poor, a prolongation of life being the utmost obtained. The earlier the animals were treated after infection the better the results; and the author believes that it is best to give numerous small doses at short intervals rather than fewer large doses at longer intervals.

The author concludes with the statement that the substance must be regarded as a valuable adjuvant in the treatment of trypanosomiasis, although its therapeutic action is not comparable to that of the arsenicals. [From the data presented this conclusion appears to the reviewer distinctly optimistic.] *W. Y.*

Keevill (A. J.). **Subsequent Histories of Six Cases of *Trypanosoma rhodesiense* Infection treated with "Bayer 205" or "Fourneau 309."**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. June 30. Vol. 28. No. 1. pp. 101–102.

This paper gives the subsequent histories of six cases of sleeping sickness treated only with "Bayer 205" and reported upon by the author in 1928 [this *Bulletin*, Vol. 25, p. 795].

In the first report it is pointed out that six patients with trypanosomes in the spinal fluid had, as the result of treatment with "Bayer 205" or "Fourneau 309" only, all remained in normal health for at least two years. The patients have been followed up carefully and their histories are shown in a Table; no further treatment had been given to any. It is seen that three of the patients (Cases 80, 85 and 86) have remained in normal health more than 8 years since infection. Of the three who died one (Case 91) survived two years and three months, one (Case 97) 5 years, and one (Case 72) 8 years after infection. The causes of death are not known, although the history suggests that Case 91 died of pneumonia. The long survival periods—5 and 8 years—make it highly improbable that the cause of death of either of the others was sleeping sickness. The longest survival period encountered by the author was in the case of a patient who had continuous treatment for 4 years and 8 months, and who undoubtedly died of sleeping sickness.

Three similar cases occurred among Keevill's 1926 patients with known survival periods of 4, 6, and 8 years, and with in each case a return to normal of the spinal fluid.

Keevill emphasizes the fact that these cases are recorded as a matter of interest only, and that it is now widely recognized by all with experience that in cases in which trypanosomes are found in the spinal fluid reliance on "Bayer 205" alone is quite unjustified, and that all such should be treated subsequently with tryparsamide.

W. Y.

Sicé (A.) & Mercier (H.). Contribution à la posologie du moranyl dans le traitement de la trypanosomiase humaine à *Tr. gambiense*. [**The Dosage of Moranyl in the Treatment of *Gambiense* Sleeping Sickness.**]—*Marseille-Méd.* 1934. Feb. 25. Vol. 71. No. 6. pp. 301–308.

This article is concerned with the question of how moranyl can be most usefully employed in human trypanosomiasis due to *T. gambiense*.

The authors state that certain investigators, especially the English, give the drug intravenously to the exclusion of all other remedies; each injection consists of 1 gm. and the dose is repeated 10 times at weekly intervals. Other workers, particularly the Germans, prefer to give 3 or 4 large doses at 2-day intervals.

The authors' experience was obtained at the Pasteur Institute of Brazzaville, where two different lines of treatment were followed. The first group of patients, who had not before received any treatment, were given moranyl alone ; in the second group of patients the drug was used to control certain blood relapses, which occurred in patients undergoing long courses of treatment with orsanine or tryparsamide.

The results obtained with the first group of patients showed that moranyl given orally or intravenously in 8 weekly doses of 1 gm. had a sterilizing effect equal to that of orsanine ; but it had the great disadvantage of producing an albuminuria which was sometimes serious.

VAUCEL has used moranyl in cases of sleeping sickness in the meningeal stage, and also for blood relapses in cases treated with arsenicals [this *Bulletin*, Vol. 28, p. 905]. Some meningeal cases improve greatly under arsenical treatment, but suffer from blood relapses, and VAUCEL found that moranyl is useful in certain of these cases ; but in those cases which show evidence of persistence of the meningeal symptoms moranyl was useless.

The authors record in detail two cases of nervous trypanosomiasis in which moranyl was combined with tryparsamide. The moranyl was given orally, on an empty stomach on waking in the morning, in a dose of 0·5 gm. An intravenous injection of 1·0 gm. of tryparsamide was given later in the morning. This treatment was given on 7 occasions at 3-day intervals. The results were favourable so far as the observations extend and only slight and transient albuminuria was occasionally seen. *W. Y.*

VON JANCSÓ (N.) & VON JANCSÓ (H.). Mikrobiologische Grundlagen der chemotherapeutischen Wirkung. I. Mitteilung : Wirkungsmechanismus des Germanins (Bayer 205) bei Trypanosomen. [**Mode of Action of Germanin in Trypanosomiasis.**]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Sept. 3. Vol. 132. No. 5/6. pp. 257–292. With 12 figs. [52 refs.]

This long and interesting paper is concerned with the mechanism of the therapeutic action of " Bayer 205 " in trypanosomiasis.

The authors point out that previous attempts to demonstrate *in vitro* a trypanocidal activity of " Bayer 205 " at all comparable with its amazing activity *in vivo* have failed, probably, as the reviewer has pointed out, because a technique has yet to be developed whereby the pathogenic trypanosomes could be maintained *in vitro* in a state of unlowered vitality for a sufficiently long period for the action of " Bayer 205 " to become manifest. After referring to the previous attempts to develop a satisfactory technique for keeping trypanosomes alive *in vitro*, von Jancsó describes his own, which is essentially a modification of that described by the reviewer and his colleagues [this *Bulletin*, Vol. 27, p. 237].

As a rule sheep serum was used ; the blood was defibrinated and then centrifuged. The serum, after being kept for a day in the ice-chest and diluted with an equal volume of Ringer solution, was filtered through a Seitz-E.K. filter. The filtration was not merely for the purpose of sterilizing the serum, but because it was found that it actually improved the serum as a nutrient medium. The filtrate was then deactivated at 60°C. for 40 minutes. Flasks made of Vitrex-glass were used in the processes, and were closed with first quality cotton wool ; they were sterilized at 130°C. for several hours.

A sterile solution of 0·02 per cent. solution of glucose in physiological saline was next prepared, and 10 cc. of the serum-glucose Ringer solution was added to each 100 cc. of the glucose solution so as to form the nutrient medium, which consequently contained 5 cc. of serum per 110 cc. The medium was then divided among small flasks so that each contained 50 cc. and the flasks were closed with cotton wool plugs.

The trypanosomes were obtained from the heart blood of rats, mice or guineapigs with moderately heavy infections and coagulation was prevented by heparin (Schering-Kahlbaum) 1 per cent. solution. The authors attach importance to this. After thorough mixing of the blood and heparin sufficient drops were added to the 50 cc. of medium to give a concentration of trypanosomes of between 200 and 1,000 per cmm. The flasks were then incubated at 37°C.–38°C. For the enumeration of the trypanosomes the Bürke counting apparatus was employed as the Thoma-Zeiss was found to be too small.

The authors state that with this technique multiplication of the trypanosomes could be observed for at least 6–10 hours and sometimes for much longer according to the strain used, and that the parasites remained alive in good condition for from 50 to 70 hours.

With the aid of this technique the authors were able to demonstrate *in vitro* a trypanocidal activity of germanin when its concentration was only 1 in 80,000, and that a concentration of 1 in 60,000 sufficed to destroy all the parasites. The trypanocidal effect was, however, manifest only after a prolonged latent period amounting to as much as 24 hours. During this latent period the trypanosomes showed no signs of any toxic effect, and multiplied just as rapidly as the controls. Even in high concentrations germanin exhibits no immediate toxic action on trypanosomes.

In this respect the action of germanin is strikingly different from that of such drugs as the arsenoxides which have an immediate effect. Apparently germanin acts, not by directly destroying vital functions, but by the production of athrepsis through interference with the nutrition of the trypanosomes.

The authors next turned their attention to the mechanism of the curative action of germanin *in vivo*. By means of splenectomy, and blocking the reticulo-endothelial system with electrocolloidal copper, they threw out of action the natural trypanocidal protective mechanism of the host, thus enabling the direct action of the drug to be studied in the living animal. It was found that the curative action depended upon the direct trypanocidal action of the chemically unchanged germanin molecule, but that the therapeutic process was rather more complicated than a simple internal disinfection.

Germanin possesses the important and peculiar property of rendering the slightly poisoned trypanosomes fit for phagocytosis by the reticulo-endothelial cells, *i.e.*, it exercises an opsonic effect. The disappearance of the parasites from the blood stream during the cure is due to a removal of the slightly damaged trypanosomes by the phagocytes in the blood sinuses of the liver, spleen and bone-marrow. This opsonic action thus greatly enhances the effect of the drug in the living animal and explains its greater action *in vivo* than *in vitro*. Nevertheless the drug can produce a cure without the aid of its opsonic power, because it is also curative in splenectomized and blocked animals. In such animals its activity is, however, distinctly less than in normal animals; and in some cases the chemotherapeutic index in normal animals was found to be 1 : 270, whilst in blocked animals it was only 1 : 135. Another observation in harmony with the above is the

time required to produce sterilization of the blood in the normal and in the blocked animal. In the former this is about 15 to 24 hours, but in the blocked animal in which the reticulo-endothelial system is put out of action and consequently the opsonic effect of the drug is not seen, the time required for sterilization of the blood is increased to 25–44 hours, which is approximately the same as that required for the destruction of the parasites *in vitro* by germanin.

In the blocked animals the same degenerative changes can be seen in the trypanosomes as in the *in vitro* observations. Characteristic among these is inhibition of division; giant forms with many nuclei, blepharoplasts and flagella appear. Sometimes as many as 60 per cent. of the parasites may be found to be in a state of division. In striking contrast the normal animal shows when treated with germanin but few abnormal forms, because as soon as the parasite commences to be damaged by the drug it is removed from the circulation by the phagocytes.

A somewhat similar opsonic effect is seen in the treatment of recurrent fever infections with solganal A & B. *W. Y.*

SINGER (Ernst), KOTRBA (Jan) & FISCHL (Viktor). Zur Frage der Kombinationstherapie. [**On the Question of Combined Therapy.**] —*Ztschr. f. Hyg. u. Infektionskr.* 1934. Aug. 16. Vol. 116. No. 3. pp. 241–247. [14 refs.]

This short and rather technical paper deals briefly with the general question of combined therapy and in particular with the question whether anything is to be gained by combining salvarsan with various heavy metals.

Ever since 1905 much attention has been devoted to the possibility of increasing the specific activity of drugs by combination. This may take one of several forms: instead of using a single drug several belonging to different chemical groups can be administered; or compounds can be synthesized which contain two active groups instead of one; or an active non-metallic compound can be combined with an active metallic salt.

With the object of throwing some light on the mechanism of action of combined therapy, the authors have considered the combination of salvarsan with inactive metallic salts, *e.g.*, coppersalvarsan and silversalvarsan; and as representative of the combination consisting of two active compounds, they employed the complex compound formed from solusalvarsan and solganal. When solutions of these are mixed together the mixture exhibits a deep red colour in contrast to the orange yellow colour of the original solutions. The therapeutic activity of each of these compounds and of the mixture was then tested on mice infected with "*Recurrens*" and nagana respectively. It was found that the mixture exerted a definitely more powerful effect than either of the components given separately.

The authors refer to the fact that in their earlier work they had devised a colorimetric method whereby they could readily estimate quantitively arsenic and other metals at the same time; for this purpose they used a spectrographic method. The metallic contents of copper-salvarsan, silversalvarsan and solusalvarsan-solganal are shown in the following table :—

Preparation.	Arsenic	Metal	Arsenic : Metal.
	%	%	
Coppersalvarsan	25·5	13·5 Cu	1 : 0·5
Silversalvarsan	19·5	12·5 Ag	1 : 0·6
Solusalvarsan-Solganal ...	10·0	18·3 Au	1 : 1·8

The results obtained with infected mice are shown in the next table. In each case half the tolerated dose was given intramuscularly, and the investigations were continued so long as fairly numerous parasites (10 per field) could be seen in the blood.

Mouse's blood after	Blood corpuscles in ccm.	Arsenic and metal in γ. Plasma.		Blood corpuscles.		Parasites.	
		Arsenic.	Metal.	Arsenic.	Metal.	Arsenic.	Metal.
Recurrens : 1/2,000 gm. coppersalvarsan per 20 gm. mouse							
30 mins.	1·35	0	0	0	0	0	0
1 hour	1·3	0	0	0	0	0·5	0
Nagana : 1/2,000 gm. coppersalvarsan per 20 gm. mouse.							
30 mins.	0·5	0	0	0	0	1·0	0
Recurrens : 1/1,200 gm. silversalvarsan per 20 gm. mouse.							
30 mins	0·7	3	3	0	1·2	0	0
1 hour	0·8	4	0	0	0	0·5	0
3 hours	0·5	3	0	0	0	0	0
5 „	0·9	4	0	0	0	0	0
Nagana : 1/1,200 gm. solusalvarsan-solganal per 20 gm. mouse.							
30 mins	0·3	20	60	3·5	2·8	0·6	0
1 hour	0·4	20	80	6·0	12·0	0·6	0·6
Recurrens : 1/1,200 gm. solusalvarsan-solganal per 20 gm. mouse.							
30 mins	1·2	21	62	5·0	4·0	0·6	0·2
1 hour	1·1	19	57	5·0	10·0	0·6	0·6

These experiments show that the various salvarsan compounds exhibit a great difference in regard to their distribution in the organism. Comparison of the above tables shows that neither in the body of the host nor in the parasite is the combination taken up as such, but that immediately after injection they are split up into their component parts, the destiny of which in the organism is different. It seems therefore clear that in the case of coppersalvarsan and silversalvarsan, the combined copper and silver is split off from the salvarsan immediately after injection, and consequently has no action on the parasite. This observation demonstrates the fallacy of the various hypotheses elaborated to explain the action of such substances, *e.g.*, the view that the antisyphilitic action of silver is enhanced in silversalvarsan because this compound, in virtue of the specific affinity of salvarsan for the spirochaetes, anchors, as it were, the silver to the parasites. The authors write that as a matter of fact, after an injection of silver salvarsan, the silver goes its own way in the organism and whether it has a special affinity for chancre tissue is a question for investigation, but it is rather improbable. Silversalvarsan can act as a combination drug, but only if the silver component exerts an influence on the

syphilitic infection and this has yet to be proved ; coppersalvarsan cannot play a part in combined therapy because copper has no spirochaeticidal action.

The authors conclude by expressing the opinion that it seems as if combined therapy will be found to have far less significance in chemotherapy than in pharmacology.

The following summary is given :—

1. Coppersalvarsan and silversalvarsan are split into their component parts after injection into the animal body; of the two components only the benzol derivative exerts a specific action on the parasite.

2. In contrast, a complex combination of solusalvarsan and solganal is described, which is also split in the body of the host into its component parts, but in this case both are taken up by the parasites. The poorer therapeutic effect of the complex combination observed is probably to be regarded as an interference phenomenon.

3. Spectrographic analysis established that these are different kinds of combination therapy. *W. Y.*

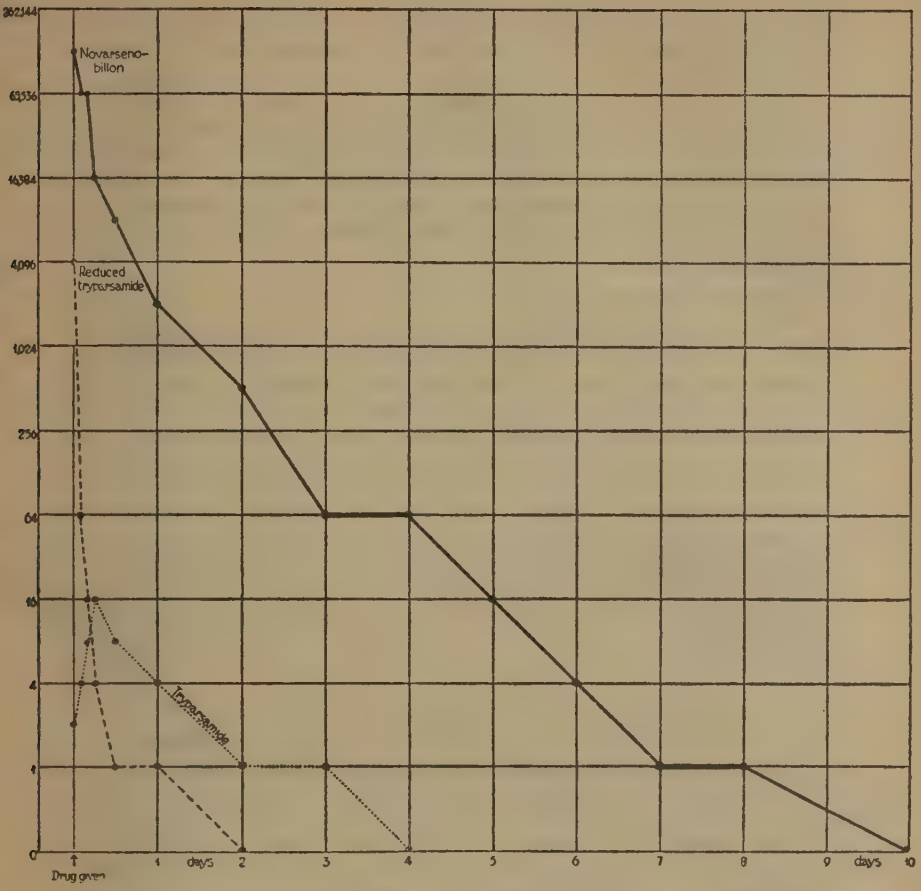
MURGATROYD (Frederick), RUSSELL (Helen) & YORKE (Warrington). **Studies in Chemotherapy. XI.—The Trypanocidal Titre of the Serum of Rabbits after the Intravenous Injection of Various Compounds of Arsenic.**—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 227–242. With 4 graphs.

Many workers have studied the problem of the length of time a drug remains in the blood after intravenous injection, but as far as the arsenicals are concerned, with not much success. The work has consisted in the quantitative estimation of arsenic in the blood, organs and excreta at stated intervals, but this method does not tell us whether the arsenic is in the blood in the form in which it was injected, or is broken down in the body, *e.g.*, whether salvarsan and tryparsamide circulate in the blood as such or are changed before they exert their specific effects, nor in what form they are eliminated.

In continuation of their previous researches the authors' object was to ascertain the trypanocidal power of the serum of rabbits after the intravenous injection of novarsenobillon, reduced tryparsamide thioglycollate and tryparsamide—typical examples of arsenobenzol compounds, aromatic trivalent and aromatic pentavalent arsenical compounds. The method essentially was the determination of the trypanocidal titre of the rabbits' serum by incubation at 37°C. of trypanosomes in nutrient medium containing various concentrations of the serum. For details of the technique the paper must be read. The results are described in the authors' summary.

" 1. Attention is drawn to the fact that there is practically no information regarding the length of time an arsenical compound remains in the blood after intravenous injection. Such information as we do possess depends upon chemical estimations of arsenic and, for reasons which are discussed, is quite inadequate for the solution of many important questions.

" 2. With the object of throwing further light on the subject a technique was devised which has enabled us to follow the variations in the trypanocidal titre of the serum after intravenous injection of rabbits with different doses of each of the three types of aromatic



Novarsenobillon ... 50 mgms. per kilo.
Reduced tryparsamide, 10 mgms. per kilo.
Tryparsamide ... 0·5 gm. per kilo.

Graph comparing the trypanocidal titre of the serum of rabbits after moderate doses of novarsenobillon, reduced tryparsamide, and tryparsamide respectively.

[Reproduced from the *Annals of Tropical Medicine and Parasitology*.]

arsenical compounds, viz., arsenobenzol, trivalent arsenical and pentavalent arsenical compounds.

"3. The effect of injection of the arsenobenzol and trivalent arsenical compounds is to confer immediately upon the serum an enormously high trypanocidal titre. This titre, which is proportional to the dose given, immediately falls—quickly at first and more slowly later—until it ultimately returns to zero. The only difference observed in the effect of the two compounds is that the fall in titre in the case of the trivalent compound is much more rapid than in that of the arsenobenzol compound.

"4. The immediate effect of injection of the pentavalent compound is to confer but a slight trypanocidal titre upon the serum. Instead of falling, however, as happens with the other two drugs, the titre steadily rises and does not attain to its maximum until approximately 6 hours

after the injection. The titre reached is, moreover, in no way comparable with the enormous titres obtained with the arsenobenzol and trivalent compounds.

" 5. Analysis of the observations made in this work suggest that the arsenobenzol and trivalent arsenical compounds owe their therapeutic activity entirely to the fact that these highly trypanocidal substances circulate unchanged in the blood stream; and that tryparsamide owes its therapeutic activity to the fact that it is gradually reduced in the blood, and possibly also in the tissues, into its corresponding trivalent compound."

Elsewhere they write :—

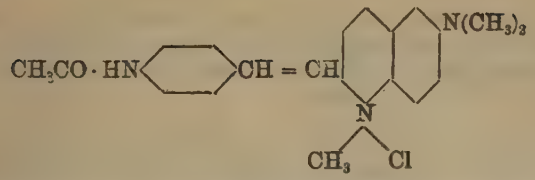
" We have already drawn attention to the remarkable speed with which the trivalent compounds escape from the blood; and, consequently, we can explain the fact that the trypanocidal titre following an injection of tryparsamide never rises beyond very modest limits (maximum observed about 128) on the ground that as fast as the tryparsamide is reduced to its trivalent form it is eliminated from the blood stream. Whether the reducing process occurs elsewhere than in the blood stream, *e.g.*, in the reticulo-endothelial cells, we do not know. Neither do we know whether the tryparsamide, which is taken up by the body cells immediately after injection of the drug, is after an interval returned to the blood stream as such, or whether it is retained in these cells until it is ultimately broken down into some simple and possibly inactive form." *A. G. B.*

Browning (C. H.) & Gulbransen (R.). **Prophylaxis of Experimental Trypanosome Infections by Chemotherapeutic Agents.**—*Jl. Path. & Bact.* 1934. July. Vol. 39. No. 1. pp. 75–82.

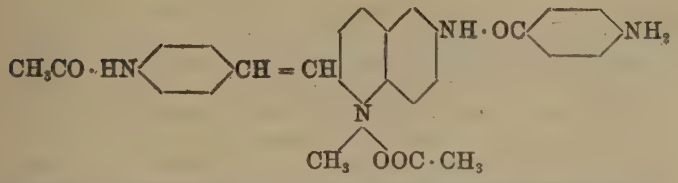
This paper is concerned with the mode of action of drugs which are known to exert a prophylactic action against trypanosomal infections.

The authors point out that the trypanocidal drugs which exhibit pronounced prophylactic action are " Bayer 205 " and certain benzoylamino quinoline styryl compounds (Nos. 245, 430 and 437 of Browning, Cohen *et al*, 1933). It is considered that prophylactic action may be due to several properties of a drug.—(1) Its excretion or destruction may occur so slowly that it circulates for a long time in the body; (2) it may form a relatively insoluble local deposit in the tissues from which small amounts continually pass into the body fluids to act upon the parasites; or (3) although rapidly excreted or destroyed the drug may act as a stimulus leading to a persistent elevation of the defensive powers of the tissue. There is, however, no evidence in support of the last mode of action.

With the styryl quinoline compounds, striking prophylactic action is associated with the presence of p-amino benzoyl (or p-dimethylamino benzoyl or p-acetylamino benzoyl) substituted in the 6-NH_2 group of the quinoline nucleus [*vide* styryl-245], and such compounds are slowly absorbed. On the other hand the analogous trypanocidal substances in which the 6-position is occupied by $-N(CH_3)_2$ [styryl-90] or $-NH{\cdot}OCH_3C$ (styryl-8) are rapidly absorbed and excreted after subcutaneous injection and exert only a brief prophylactic action.



2(*p*-acetylamino styryl)-6 dimethylamino quinoline methochloride (styryl-90)—prophylactic action brief.



2(*p*-acetylamino styryl)-6(*p*-amino benzoylamino) quinoline methoacetate (styryl-245)—prophylactic action prolonged.

In their experimental work the authors used three strains of *T. brucei* obtained from MESNIL and one strain from WORMALL in Uganda. In two tables the prophylactic action for mice of Bayer and of styryl-245, respectively, are shown. With " Bayer 205 " it was found that 1 cc. of a 1 in 200 solution protection lasted less than 3 months and after a dose of 1 in 1,000 solution about 2 months. Experiments with styryl-245 showed that 1 cc. of a 1 in 200 or 1 in 250 solution confers on mice longer protection than any other known substance. In some cases complete protection for almost a year was observed.

The authors state that styryl-245 owes its protective power to the fact that when a watery solution is injected subcutaneously a local deposit forms, which is accompanied by considerable reaction of the connective tissue elements ; the dye is fixed intracellularly to a great extent and still persists at the site after a year or longer. The amount in circulation at any time is very minute, but nevertheless sufficient is absorbed to prevent infection on subsequent inoculation with trypanosomes, or, when the drug is injected after inoculation, to cure the established infection. *W. Y.*

CHRISTISON (May H.). Ueber chemotherapeutische Versuche bei der Rattentrypanose (*Trypanosoma lewisi*). [**Chemotherapeutic Experiments on** *T. lewisi* **infected Rats.**]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Aug. 7. Vol. 132. No. 3/4. pp. 228–237. [34 refs.]

The paper contains a summary of the therapeutic results obtained with 21 pyridin compounds of arsenic and with certain other substances, including two arsenostibio-compounds, on infections due to *T. brucei*, *Spirochaeta crocidurae*, *Bac. rhusiopathiae* and *T. lewisi*, respectively.

Of the arsenopyridin compounds only one, *viz.*: Br 23, *i.e.*, 2-pyridon-3-amido-5 arsinic acid exercised a weak action on *T. lewisi* infections. The arsenostibio-compound Sdt 386 B, which is so active in Bartonella infections, likewise exerted only a slight action on *T. lewisi*. *W. Y.*

Browning (C. H.), Cappell (D. F.) & Gulbransen (R.). **Experimental Infection with *Trypanosoma congolense* in Mice: the Effect of Splenectomy.**—*Jl. Path. & Bact.* 1934. July. Vol. 39. No. 1. pp. 65–74. [19 refs.]

As a preliminary to studying the chemotherapy of *T. congolense* infections the authors have passed a strain of the parasite repeatedly through mice with a view to accommodating it so far as possible to this host, and they have also examined the effect of splenectomy and blockade.

Extended observations over several hundred passages in mice showed that the parasites were incapable of developing the high virulence for that species which is characteristic of *T. brucei*. Many of the mice of the first 50 passages failed to become infected. From the 83rd passage onward infection always occurred, but in only about a fourth of the animals was there a progressive increase of the parasites and the infection took an acute course; in the remainder the infection took a relapsing, or, less frequently, a chronic course. The incubation period was but slightly shorter in the later passages than in the earlier ones.

The animals which resisted the first large inoculations were shown to be abnormally resistant as tested by their behaviour on reinoculation, but after repeated re-inoculations they finally became infected. Spontaneous cure was very rarely seen.

Neither splenectomy nor combined splenectomy and blockade with iron sugar produced any definite alteration in the course or severity of the infection of *T. congolense* in mice. *W. Y.*

Corson (J. F.). **The Infectivity of *Trypanosoma rhodesiense* in Relapses after Treatment with "Bayer 205."**—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 225–226.

The experiment described in this paper was undertaken with the object of throwing light on the question whether in sleeping sickness the blood during relapses after "Bayer 205" can infect tsetse flies.

In order to eliminate doubt about relapse or re-infection in the case of natives, it would be necessary to detain them in a fly-free place until a blood relapse occurred. Owing to the temporary absence of facilities for doing this, the author thought it worth while to make an experiment with laboratory animals.

A rat was bitten by a tsetse fly infected with *T. rhodesiense* on February 18th, and trypanosomes appeared in its blood on the 5th day onwards. On 5th March the blood was inoculated into 3 rats, all of which became infected. Fourteen days later, when trypanosomes were numerous in the blood, each of these 3 rats was given a subcutaneous injection of 0·02 gm. of "Bayer 205" per kilo. of body weight. The trypanosomes disappeared from the peripheral blood in each case from March 21st to 24th, reappearing on March 25th for a few days and again disappearing for various periods. On March 28th other rats were sub-inoculated from these 3 animals and all became infected. Laboratory-bred *G. morsitans* and *G. palpalis* were fed on the first 3 rats on March 27th, 28th and 29th, and afterwards on a clean rabbit. On April 17th the flies were transferred to a clean guineapig which became infected.

These experiments show that *T. rhodesiense* in rats, during a relapse after treatment with "Bayer 205," was transmissible both by direct inoculation and by cyclically infected tsetse flies. *W. Y.*

DUKE (H. Lyndhurst). **On the Transmissibility by *Glossina* of *Trypanosoma brucei*, *T. rhodesiense* and *T. gambiense*, with Special Reference to Old Laboratory Strains.**—*Parasitology*. 1934. June. Vol. 26. No. 2. pp. 153–162. [14 refs.]

This paper records the result of an investigation of the transmissibility of certain strains of trypanosomes of the polymorphic group; it deals particularly with strains which have been maintained for a long period in the laboratory away from any contact with tsetse.

In his historical introduction Duke points out that BOUET and ROUBAUD (1910) found that they could not transmit by Glossina strains of *T. brucei*, *T. evansi*, and *T. gambiense*, which had been obtained from the Pasteur Institute in Paris. KLEINE and FISCHER (1913) in East Africa were unable to transmit certain strains of *T. gambiense* by Glossina. REICHENOW (1921) reported that certain strains of *T. gambiense* in man himself were not transmissible, and during recent years much work has been done on this subject by Duke himself.

The strains examined in the present work were as follows:—

No. 1. T. gambiense, *strain V*. First isolated from man early in 1926 and found to possess an unusual degree of transmissibility by *G. palpalis*.

No. 2. T. gambiense, *strain "Adero."* Isolated from a native of the Uganda Protectorate in January, 1933.

Nos. 3 *and* 4. T. rhodesiense, *"Liverpool" strain*. This was sent to Duke by the Reviewer. It was isolated from man in 1923, and the arsenic-fast variant, No. 4, was prepared in Liverpool.

No. 5. T. brucei, *strain "Hamburg alt."* This is the strain used by Schilling and Schreck (1930) in their work on the stability of acquired characters in trypanosomes, experiments performed in 1912–14 and published in 1930. The remarkable feature of Schilling's work with this strain appears to be the ease with which it was passed through tsetse. The Reviewer has already commented on this curious fact [this *Bulletin*, Vol. 28, pp. 894–5].

No. 6. T. gambiense, *strain "Braun."* Isolated at Hamburg in February, 1920, from a patient from Fernando Po.

No. 7. T. gambiense, *strain "McA."* Supplied by Professor Thomson and isolated from a European in November, 1921.

No. 8. T. brucei, *strain "Hornby mild."* Isolated in October, 1930, from an ox by Mr. Hornby at Mpwapwa.

No. 9. T. brucei, *strain "Hornby virulent."* Isolated from a heifer in April, 1927.

No. 10. T. gambiense, *strain "Br."* Supplied by Professor Thomson and isolated from a European in June, 1930.

Duke summarizes the result of his work as follows:—

"1. The following strains produced no infection in any of the laboratory-bred *Glossina* used in their examination; the total number of flies dissected is given for each strain:—

T. gambiense, strain V, Uganda, isolated in 1926 ...	548
T. gambiense, strain Adero, Uganda, isolated in Jan., 1933	1,642
T. rhodesiense, Liverpool, isolated in Jan., 1933 ...	750
T. rhodesiense, Liverpool, arsenic-fast variant	1,166
T. brucei, "Hamburg alt" from Berlin; isolated over 30 years ago	2,452

"Some of the flies used in testing each of these strains were kept at 95–97°F. during their infecting feeds.

" 2. *T. gambiense*, strain ' Braun,' isolated in February, 1920, gave two ' gut only ' infections in 1,137 flies. *T. gambiense*, strain ' McA,' isolated in 1921, produced one very light infection, of the intestinal tract only, in 1,410 flies employed. This infected fly died on the 27th day after its infecting feed.

" *T. brucei*, strain ' Hornby mild,' isolated at the end of 1930, gave three infections of the intestinal tract only in 1,443 flies used. Some of the flies employed on these three strains were kept during their infecting feeds at 95–97°F., but the infected flies came from boxes kept at room temperature throughout.

" It will be seen that all the strains hitherto summarized are, as far as these tests are concerned, non-transmissible by Glossina, and the majority are no longer capable of infecting even the intestine of the fly.

" 3. *T. brucei*, strain ' Hornby virulent,' isolated in April, 1927, from a heifer, and found by Corson in 1931 to be readily transmissible by *G. morsitans* or *G. pallidipes* (or both), 4½ years after its first isolation (Corson, 1932). A month or so later this strain was found at Entebbe to be still feebly transmissible by *G. palpalis* and somewhat more readily by *G. morsitans*, although much less so than in Corson's experiments.

" 4. Strain ' Br,' considered by Prof. J. G. Thomson to be a *T. gambiense* showing some resemblances to *T. rhodesiense*, when examined at Entebbe some three years after its isolation from a European in West Africa, proved to be still infective to both *G. palpalis* and *G. morsitans* though only very feebly transmissible. 4,272 laboratory-bred flies were used in the examination of this strain : 74 of these developed infection of the intestine, and only one a gland infection—a *G. palpalis* dying on the 40th day after its infecting feed. Flagellates were numerous in the glands of this fly.

" 5. The behaviour of the ' Hornby virulent ' strain of *T. brucei* and of strain ' Br. ' suggests that completion of the cycle in the fly may be delayed beyond the 25–30 days usually sufficient for East African strains, and it is possible that this delay may be a feature characteristic of strains whose transmissibility by tsetse is undergoing reduction. On the other hand, the solitary infective fly obtained with strain ' Br. ' had a heavy gland infection which had in all probability been present at least for several days before the death of this insect.

" 6. A strain freshly isolated from a native who was infected on or near the northern shores of Lake Victoria failed to infect any of 1,642 *G. palpalis* used in its examination, although a number of these flies were kept at 95–97°F. during their infecting feeds.

" 7. The results of the investigations described in this paper lend some support to the opinion already formed as the result of numerous experiments with the polymorphic group of trypanosomes, namely that *T. brucei* (and, as far as can be seen, *T. rhodesiense*) is less prone than *T. gambiense* to lose touch with Glossina.

" It may be that the stability of this character in *T. brucei* is an expression of a more perfect adjustment to environment than is possessed by *T. gambiense* ; the latter trypanosome, which is essentially dependent on man, having not yet attained biological equilibrium in this its principal mammalian host." *W. Y.*

DUKE (H. L.). **Studies on the Factors that may influence the Transmission of the Polymorphic Trypanosomes by Tsetse.**—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. p. 244.

This note draws attention to an omission in a previous paper by the author [this *Bulletin*, Vol. 31, p. 565]. In the paper in question the description of the maintenance of Strain XXXIII opens with

the statement: "In the main series this strain underwent 10 consecutive cyclical passages." Actually the Table only shows 8 passages. In the present note the Table is completed, showing that the strain was cyclically transmitted through two more monkeys. The extra evidence confirms, in the author's opinion, the reduction in transmissibility suggested by the behaviour of the trypanosomes in the two previous monkeys and is therefore important to the thesis of this particular study. *W. Y.*

Duke (H. Lyndhurst), Mettam (R. W. M.) & Wallace (J. M.). **Observations on the Direct Passage from Vertebrate to Vertebrate of Recently Isolated Strains of *Trypanosoma brucei* and *Trypanosoma rhodesiense*.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. June 30. Vol. 28. No. 1. pp. 77–84. [29 refs.]

This paper contains observations on the direct passage from vertebrate to vertebrate of recently isolated pathogenic trypanosomes. It is divided into three sections each dealing with a different mode of transmission.

i. *Transmission of* T. brucei *to healthy cats as a result of digestion of carcases of infected rats.*—Bruce (1897) was the first to show that an animal might contract trypanosomiasis as a result of devouring blood or flesh of a nagana carcase; and this observation was soon confirmed by numerous other workers. Duke's experiments consisted in feeding two kittens with the carcases of rats, the blood of which swarmed with *T. brucei*. Both kittens became infected and parasites were first discovered in their blood in 11 and 12 days respectively.

ii. *Direct transmission by* Stomoxys *and* Glossina.—A brief summary is given of previous work on this subject. Duke himself found that *T. rhodesiense* was readily transferred from an infected to a healthy monkey by the process of interrupted feeding; 7 to 10 wild Stomoxys were used in the experiment.

iii. *The passage of* T. rhodesiense *through the placenta.*—Five guineapigs with *T. rhodesiense* in their peripheral blood gave birth to young which were found to be infected. The young of another guineapig born 3 days after the date of the infection of the mother (by fly bite) did not become infected, although they were suckled by the infected parent until her death. Three guineapigs infected with *T. gambiense* for 40 days before parturition produced healthy young.

Experiments designed with the object of determining whether fleas and lice can act as mechanical vectors of *T. brucei* produced negative results. *W. Y.*

Corson (J. F.). **The Cerebro-Spinal Fluid of Some Small Antelopes Infected with *Trypanosoma rhodesiense*.—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 243–244.

In this note the author records the results of the examination of the cerebrospinal fluid of 8 adult dik-diks and one young duiker experimentally infected with *T. rhodesiense*. The cerebrospinal fluid was obtained by suboccipital puncture either immediately after death from the disease, or, more frequently, after death from chloroform

when the animal was dying. These interesting observations are summarized in the following table :—

Animal	Infected on	Infected by	Died on	Duration of disease	Trypanosomes in blood at death	Cerebro-spinal fluid	
						Living tryps.	Cells
1. Dik-dik	23. 9.33	Tsetse bite	6. 3.34	164 days	few	135	8,000
2. ,,	2.10.33	,, ,,	19.10.33	17 ,,	numerous	0	3
3. ,,	21.10.33	,, glands	3. 3.34	133 ,,	few	21	8,000
4. ,,	26.10.33	,, ,,	25.12.33	55 ,,	numerous	4	400
5. ,,	23.11.33	,, bite	5. 2.34	74 ,,	not exam.	0	many
6. ,,	27.11.33	,, ,,	31.12.33	34 ,,	numerous	29	many
7. ,,	22.12.33	,, ,,	22. 3.34	90 ,,	none	22	678
8. ,,	21. 1.34	Inoculated from No. 5	24. 3.34	62 ,,	present	6	173
9. Duiker	27. 1.34	Tsetse bite	6. 3.34	38 ,,	few	5	292

N.B.—Dik-dik 5 died the night before the suboccipital puncture was made.

These animals were caught in a tsetse-free locality and were kept in captivity in a state of good health some months before being infected. Dik-diks and duiker are known to live in tsetse-infected regions, and they are found to frequent farms about dusk. Corson remarks that it is hard to understand how they could survive in sleeping sickness areas unless a combination of relative slight exposure to tsetse bites and habituation to mild strains of *T. brucei* gives them an acquired and selected resistance. It would be interesting to examine the blood of these animals in tsetse-infested regions. *W. Y.*

Reichenow (Eduard). Die Züchtung der pathogenen Trypanosomen. [**Culture of Pathogenic Trypanosomes.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. July. Vol. 38. No. 7. pp. 292–302. With 6 figs. [12 refs.]

This paper records methods by which *T. gambiense*, *T. congolense* and *T. cruzi* were successfully cultured.

The technique employed was essentially the same as that described in 1929 by the author's pupil, Razgha [this *Bulletin*, Vol. 27, p. 244]. The medium consists of citrated human blood and Ringer solution. A series of tapered tubes (centrifuge tubes) containing 1 cc. of Ringer solution, made with 0·6 per cent. sodium chloride, is sterilized, and then to each is added 1 cc. of citrated blood. The medium thus consists of 25 per cent. blood, 25 per cent. sodium citrate solution and 50 per cent. Ringer solution. It is not necessary to deactivate the blood, but it is advantageous to keep the medium 2 or 3 days in the ice chest before use. The optimum temperature for culture is 24°C. and subinoculations should be made every 14 days, although in some cases every 4 weeks suffices.

It is recalled that Razgha obtained successful cultures only with recently isolated strains of *T. gambiense*. In his first experiments with *T. gambiense* Reichenow employed the strain "*Gambiense G*," which he formerly had maintained in culture for 111 days. He succeeded in culturing this strain again $1\frac{3}{4}$ years after it was isolated

from man. The cultures were good and were maintained until the 19th passage when they died out. About the same time cultures were made from another strain of *T. gambiense* which was freshly isolated from man. These were also successful and were maintained until the 7th passage when they died out. In an endeavour to explain the reason why the cultures died, the author endeavoured to start new cultures from the same strains, which in the meantime had been maintained in animals. These later attempts were practically failures and it thus became evident that they had lost their cultural capacity. This is not so strange in the case of "*Gambiense G,*" which by this time had been isolated from man for 2½ years, but the second strain "*Gambiense Sche*" was only 6 months old. Reichenow, however, observes that the patient had been infected for at least 9 months before the strain was isolated, and he remarks that it has been repeatedly pointed out by DUKE and others that prolonged sojourn of a strain in one vertebrate host may interfere with its capacity to develop in the invertebrate host. The author considers that there is a parallelism between a strain's capacity to be cultured and its power to infect Glossina. The cultural forms of *T. gambiense* are described; these are similar to the forms which are seen in the gut of the tsetse fly.

Experiments were next conducted with a 9-year-old strain of *T. congolense*. At first goat's blood was used in the culture medium and the immediate results were excellent, but the first subculture practically failed, only a few tubes exhibiting feeble growths. When, however, human blood was used instead of goat's blood, the cultures were equally good and subcultures were successful. The culture has now been maintained to the 10th passage over a period of 4 months. Reichenow points out that it is strange that human blood is a good culture medium for *T. congolense* in view of the fact that it has a definite therapeutic action in rats infected with this parasite. Again, the culture forms were similar to the developmental forms found in the gut of Glossina.

T. cruzi was found to grow better in the blood Ringer medium than in NN-Agar medium, but it was necessary to add a little glucose to the Ringer solution. *W. Y.*

PACKCHANIAN (Ardzroony). **Experimental** *Trypanosoma brucei* **Infection and Immunity in Various Species of Peromyscus (American Deer Mice).**—*Amer. Jl. Hyg.* 1934. July. Vol. 20. No. 1. pp. 135–147. [18 refs.]

This paper records the pathogenicity of *T. brucei* for a number of species, subspecies and hybrids of American rodents belonging to the genus *Peromyscus*.

The trypanosome used was the strain of nagana sent to England by BRUCE in 1896, and thence to McGill, where it has been maintained ever since in guineapigs. At the time of the experiments it killed guineapigs in 16 to 22 days, and rats and mice within a week.

Peromyscus c. californicus, P. c. insignis, P. c. eremicus, P. e. anthonyi and *P. p. polionotus* all contracted an acute infection and died within 10 days. *P. maniculatus* and its various subspecies exhibited a high resistance to the disease and contracted a subacute infection with

crises and relapses, the duration of the disease being over 80 days. A number of hybrids developed subacute or chronic infections.

W. Y.

FINE (J.). **The Influence of Avitaminosis on the Course of Trypanosome Infection.**—*Jl. Hygiene.* 1934. June. Vol. 34. No. 2. pp. 154–156.

In the experiments recorded here the course of a *T. brucei* infection in rats exhausted of their Vitamin A reserves was compared with that of a similar infection in rats provided with Vitamin A, but otherwise receiving the same diet.

The results of these experiments, which are summarized in a table, show that in both groups trypanosomes appeared in the blood 3 days after inoculation ; the average survival for the rats receiving Vitamin A was 9 days, and for those deprived of Vitamin A 8·8 days.

The conclusion reached is that there is no significant difference between the course of *T. brucei* infection in the rat exhausted of Vitamin A and that in the rat adequately supplied with this Vitamin. [It seems to the reviewer that it would be dangerous to generalize from this work that lack of Vitamin A has no influence on trypanosomal infections. It is unfortunate that the author chose such an acute infection. The control animals died so quickly that those deprived of Vitamin A could hardly be expected to die more quickly. It would be interesting to repeat this work with a more chronic infection.]

W. Y.

UNIVERSIDAD BUENOS AIRES MISIÓN DE ESTUDIOS DE PATOLOGÍA REGIONAL ARGENTINA JUJUY. 1934. Publicación No. 16. pp. 3–10. With 3 figs. (1 map) ; pp. 11–20. With 5 figs. Investigaciones sobre la enfermedad de Chagas. I. Primer caso agudo de la enfermedad de Chagas comprobado en la provincia de Santiago del Estero [RAIMONDI (Silvio) & FEIJOÓ (Enrique J. Canal)]. [**The First Acute Case of Chagas's Disease recorded in the Province of Santiago del Estero.**] II. Comprobación de formas agudas de la enfermedad de Chagas en Añatuya (Santiago del Estero) [MAZZA (Salvador) & GUERRINI (F. Z.)]. [**Acute Forms of Chagas's Disease in Anatuya (Santiago del Estero).**]

I. The patient was a boy of 8 years of age, who presented the typical symptoms of this infection in a mild, though acute, form. In his home *Triatoma infestans* was found in large numbers. A map of the Province and district accompanies the article, but is so reduced that with few exceptions the names are illegible even with a lens.

II. Accounts of further cases of this disease in the same Province. The author calls attention to the relative large proportion of patients who die of " syncope "—" the heavy tribute which the inhabitants of the district pay to infection by *Schizotrypanum cruzi.*" During the three years 1931–33, out of 233 deaths 22 or 10·6 per cent. died from " cardiac syncope " ; the actual figures being, total 79, 72, and 82 respectively, syncope 5, 9, and 8, or 6 and 12 and 9 per cent.

H. H. S.

Universidad Buenos Aires Misión de Estudios de Patología Regional Argentina Jujuy. 1934. Publicación No. 17. pp. 3–11. With 3 figs.; pp. 12–16. With 4 figs. pp. 17–23. With 1 fig.; pp. 23–28. With 4 figs.—Investigaciones sobre la enfermedad de Chagas. I. Casos agudos benignos de enfermedad de Chagas comprobados en la provincia de Jujuy [Mazza (Salvador)]. [**Mild Acute Cases of Chagas's Disease in the Province of Jujuy.**] II. Hallazgo del gato como portador natural del *Schizotrypanum cruzi* en la provincia de Jujuy [Mazza (Salvador)]. [**The Cat as a Natural Host of *Trypanosoma cruzi* in the Province of Jujuy.**] III. Comprobación de otra forma aguda de la enfermedad de Chagas en la provincia de Jujuy [Mazza (Salvador) & Almaraz (Pablo)]. [**Another Benign Acute Case of Chagas's Disease in Jujuy.**] IV. Difusión de la infección natural por *Schizotrypanum cruzi* en perros de la provincia de Jujuy [Mazza (Salvador)]. [**Spread of *T. cruzi* by Dogs in Jujuy.**]

I & III. The first and third of these papers deal with acute cases of infection by *T. cruzi* but of a comparatively mild character. All those quoted were associated also with malarial infection, usually *P. vivax* or *P. falciparum*. Cases are liable to be overlooked because when examination of the blood has revealed malaria parasites, the diagnosis of paludism is made and investigation of the blood is not pursued further. There is even more excuse for missing the trypanosome infection if the quartan parasite is found for this type of malaria in this district is often associated with oedema of the face and splenomegaly. [Perhaps further study may show that these patients suffer from the dual infection of malaria and trypanosomiasis and that the quartan parasite alone does not so often exhibit its presence by these symptoms.]

II. Previous investigators have examined cats in the dwellings inhabited by patients suffering from *T. cruzi* infection but with negative results as regards the animals harbouring the parasite. The author, however, found a 2-months-old kitten infected and microphotographs show well the presence of the trypanosome "cyst" in the thigh muscles; they were not found elsewhere in the body.

IV. Further proof that dogs, in particular puppies, are carriers of *T. cruzi*. *H. H. S.*

Chagas (Evandro). Atténuation de la virulence du *Trypanosoma cruzi* par son passage dans l'organisme humain. [**Attenuation of the Virulence of *T. cruzi* by Passage through Man.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 26. p. 1153.

An observation is recorded which, in the author's opinion, indicates that the virulence of *T. cruzi* is attenuated by passage through man. The strain was obtained from a patient suffering from the chronic cardiac form of the disease. From this patient a guineapig was infected and its blood was then injected into a patient suffering from hopeless cancer. The Machado-Guerreiro reaction (fixation-reaction) was positive on the 10th day and inoculation of the blood into a normal guineapig on the 8th day produced infection. Trypanosomes were found in the peripheral blood only on the 37th day. After 2½ months, the Machado-Guerreiro reaction being still strongly positive and the blood infective for guineapigs, a second cancerous patient

was subinoculated from the first. The result was negative. Apparently the first patient had parasites in his blood because it infected guineapigs, but they were so attenuated that they were unable to produce infection in man. *W. Y.*

DUNN (Lawrence H.). **Attempts to transmit *Trypanosoma cruzi* Chagas with Ticks of the Genus Ornithodoros.**—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 283–289.

The author has examined experimentally the capacity of *Ornithodoros talaje* and *O. venezuelensis* to transmit *T. cruzi*. Four lots of the former ticks were fed on infected guineapigs, and later on 15 healthy guineapigs; all remained negative. Injection of macerated ticks likewise failed to infect. Several batches of immature and adult *O. venezuelensis* were fed on an infected guineapig and later on healthy animals, but failed to infect; some of the ticks were then macerated and injected into 7 guineapigs, all of which became infected.

From this work it is concluded that neither *O. talaje* nor *O. venezuelensis* commonly transmits *T. cruzi*, but that in the latter species of tick *T. cruzi* may develop and persist for more than six months. *W. Y.*

DUNN (Lawrence H.). **Notes on the Reduviid Bug, *Eratyrus cuspidatus* Stal., naturally infected with *Trypanosoma cruzi* Chagas found in Panama.**—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 291–292.

A third species of haematophagous bug of the family Reduviidae has been found in Panama with a natural infection of *T. cruzi*. The bug in question was examined by BARBER at the United States National Museum, who identified it as *Eratyrus cuspidatus* Stal. This species has been found previously only in Columbia and Venezuela. *W. Y.*

RISQUEZ (Jesús Rafael). Tripanosomosis de los reduvideos de Venezuela. [**Infection of Reduviid Bugs by Trypanosomes in Venezuela.**]—*Gac. Med. de Caracas.* 1934. Apr. 15. Vol. 41. No. 7. pp. 97–100. [20 refs.]

To the author were sent hemiptera from 24 localities in Venezuela; from 20 they arrived in a fit state for examination. Forms of *T. cruzi* have now been found in 8 species of Triatoma, *viz.*: *T. dimidiata, T. geniculata, T. infestans, T. protracta, T. rubrofasciata, T. sanguisuga, T. sordida, T. vitticeps*; also in *Rhodnius prolixus* and in *Eratyrus cuspidatus*. In two other species of Triatoma [not named] parasites similar to *T. cruzi* have been described and these will very likely prove to be carriers also. *H. H. S.*

MAZZA (Salvador). Los "gigantocitos quisticos" en los animales experimentalmente infectados con *Trypanosoma cruzi*. [**"Cystic Gigantocytes" in Experimental Infections with *T. cruzi*.**]—*Arch. Ital. Sci. Med. Colon.* 1934. June 1. Vol. 15. No. 6. pp. 403–410. With 3 figs. [17 refs.] English summary (3 lines).

In 1929 MAGARINOS TORRES and PENNA DE AZEVEDO reported finding in the myocardium of the armadillo aggregations of developmental forms of *T. cruzi* within large cells [this *Bulletin*, Vol. 27,

p. 247]. These cells they regarded as the perivascular histiocytes of small arteries. They have now shown that the same may be seen in the myocardium and the thyroid of dogs experimentally inoculated with the faeces of the Triatoma vector, or with the blood of human cases of American trypanosomiasis. *H. H. S.*

NASH (T. A. M.). **The Efficacy of Bush Clearing as a Method of Tsetse Control.**—*West African Med. Jl.* 1934. Apr. Vol. 7. No. 4. pp. 137–139.

Up to date bush clearing remains the only certain method of freeing an area from tsetse fly, and consequently it is a subject of great importance. In this paper the author discusses the various types of clearings now employed.

These are of two kinds, aggressive and defensive :—

(1) *Aggressive Clearings.*—These are directed towards clearing areas by reclaiming a piece of land and rendering it untenable to fly. The tsetse survey made at the end of the dry season often shows that flies which have been menacing a piece of country during the rains have come from a small dry-season concentration area. The removal of this fly sanctuary would greatly reduce the number of tsetse for a considerable distance. The author points out, however, that before steps are taken in this direction, it is important to survey the district thoroughly lest there be alternative sanctuaries available to the fly. Failing better methods of tsetse extermination, aggressive clearing should be our ultimate objective, but at present all available resources must be reserved for the more urgent defensive clearings.

(2) *Defensive Clearings.*—These aim at safeguarding the population during the course of their normal work, or whilst travelling along the main routes. In other words, they aim at reducing the man–fly contact to negligible proportions. Often it is only necessary to clean a strip of vegetation along a river for half a mile in length by 10 yards in width in order to reduce enormously the man–fly contact. It is, of course, essential before embarking on a program of clearing to identify the local tsetse, as the width of clearing depends mainly upon the species and to a lesser extent upon local conditions.

The author considers each of the three common species separately :—

(*a*) *Glossina palpalis.*—If a fly-infested stream or river passes through cultivation, all heavy forest and thicket must be removed over that part of the stream's course which passes through cultivation over a distance of a quarter of a mile after the river has entered the surrounding bush. Tall mango trees in the village near the river should be viewed with great distrust and carefully inspected for tsetse during the early dry season, and if fly are found these trees should be cut down or pollarded. It is, of course, essential that the clearings should be constantly cleaned. When a fly-infested river crosses a road, the vegetation should be cleared for a distance of a quarter of a mile on each side of the ford. It is difficult to lay down hard-and-fast rules in the case of *G. palpalis*, but as normally the insect is dependent on heavy shade, small clearings are very efficacious.

(*b*) *Glossina tachinoides.*—This species is much easier to deal with. Often all that is necessary is to cut down the thin fringe of riverine vegetation which clothes the bank of the local stream ; this fringe may be only 10 yards in width and composed of quite small trees.

G. tachinoides never flies far from home, and, consequently, it is unnecessary to extend the clearings of the river banks beyond the limit of cultivation. When *G. tachinoides* infests the main route, all trees should be cut down for a depth of 100 yards on each side of the road, and all small thickets up to a distance of 300 yards.

(*c*) *G. submorsitans*.—No attempt should be made to clear against this species, unless the matter is very urgent; it is far better to remove the population if possible. *G. submorsitans* will cross the best of clearings, even if it is a mile in width.

The author next discusses the subject of clearing technique, and summarizes his points as follows:—

" (1) The species of tsetse must first be identified.
" (2) The clearing must be made early in the dry season.
" (3) European ring-head axes should be used.
" (4) The slash should be loosely pulled over the stump, which should first have been packed with grass.
" (5) The clearing must be protected from fire until late in the dry season, when it should be burnt with a strong following wind.
" (6) The clearings must be cleaned annually at the end of the rains, and river banks and river beds kept free of all regrowth." *W. Y.*

MORRIS (K. R. S.). **The Bionomics and Importance of** *Glossina longipalpis*, **Wied., in the Gold Coast.**—*Bull. Entom. Res.* 1934. Sept. Vol. 25. Pt. 3. pp. 309–335. With 11 figs. & 2 maps in text. [15 refs.]

It appears that *Glossina longipalpis* is an important vector of the trypanosomes which attack man* and animals in West Africa. Little or nothing is known of its biology, which is the subject of the present paper.

In the Gold Coast and probably in other areas, the distribution of the insect is limited to "transition forest," and it avoids both the wet equatorial forests and the arid savannah. The author's detailed studies of the insect have been made in a small isolated patch of suitable forest close to Takoradi. In this area he found that the commonest food of the insect is the blood of small antelopes, and that when they were driven out the fly became extremely rare. Indeed, it is evident that the flies which sought human blood are not a fair sample of the wild population, for only a small proportion of the females are pregnant at any time of the year. The author devoted much of his time to a study of climate, and he endeavoured to relate the numbers of flies caught to light, temperature, humidity and rainfall. Within the limited range of conditions which prevailed at Takoradi, it was clear that temperature had a greater effect than the other factors. The author employs correlation coefficients and finds high and significant positive correlation with temperature, and less high but significant correlation with evaporation and sunshine. He observes, moreover, that there is a higher correlation between fly numbers and the temperature of the same week than between fly numbers and the temperature of the previous week; from this one may perhaps conclude that the effect of temperature is rather on the activity of the insects

* The evidence that *longipalpis* is a vector of human trypanosomiasis appears to be slight.—Ed.

themselves than on the size of the Glossina population. The author realizes the limitations of his method, and points out that the influence of temperature may be predominant only in the rather uniform climate in which his studies were made; indeed, he is of opinion that in the wider problem of the geographical distribution of the insect, humidity is at least equally important. He finds also that investigating the effect of climatic factors upon the fly is complex not only because the number of factors is great, but also because the flies' activities exhibit a daily rhythm.

It was found that flies in nature were infected with *Trypanosoma gambiense, congolense* and *vivax*, and it appears that the fly may become more important in relation to human trypanosomiasis as the agricultural development of the Gold Coast proceeds. It seems that the villager continually shifts his area of cultivation, burning forest and leaving it to regenerate into lower secondary growth which is more suited to this insect. The view is expressed that the native should be encouraged to cultivate a compact area and to keep land in cultivation: this implies the use of manure and of rotation of crops. It seems that if cultivation can be centred round villages and maintained continuously in certain areas, the contact between fly and man will be reduced and the menace of trypanosomiasis lessened. *P. A. Buxton.*

Lewis (D. J.). **The Behaviour of the Larvae of Tsetse-Flies before Pupation.**—*Bull. Entom. Res.* 1934. July. Vol. 25. Pt. 2. pp. 195–199. With 1 plate. [18 refs.]

By comparison with the extremely active larva of the house-fly or the bluebottle, that of a tsetse-fly, which is adapted to an intra-uterine life, is on extrusion a slow-moving creature, which crawls and burrows by means of peristaltic movements and longitudinal contractions, possibly aided in some degree by its soft and tiny antenno-maxillary appendages. It is believed (by Swynnerton) that the pregnant female tsetse drops her offspring in haphazard fashion, and is not guided by selective instinct to a patch of suitable ground in which the larva may burrow. Yet the latter, in order to be certain of escaping the attacks of predators and parasites, and securing protection from the fatal results of exposure to the sun, must needs be extruded on to soil in which it can burrow rapidly, and to a sufficient depth. If less fortunate on extrusion, it must crawl until it finds suitable soil in which to burrow.

The observations here described were made at Gadau, in Northern Nigeria, and the species experimented with were *Glossina morsitans*, form *submorsitans* and *G. tachinoides*. When trays respectively filled with wood ash, and with sifted sand of different coarseness, were placed beneath breeding cages containing tsetse-flies, so that the larvae produced fell on to the contents of the trays through coarse wire gauze, it was found that "burrowing efficiency has little or no relation to the weight of the larva." In the case of both species, "more larvae burrowed in coarse than in fine sand, and more in sand than in wood ash." Fine sand with pebbles was readily burrowed into.

A summary is given of statements by previous investigators concerning the burrowing powers of the larvae of various species of Glossina, and the nature of the soil in breeding places.

E. E. Austen.

PERLA (David). **The Protective Action of Copper and Iron against *Trypanosoma lewisi* Infection in Albino Rats.**—*Amer. Jl. Hyg.* 1934. Mar. Vol. 19. No. 2. pp. 514–520. [13 refs.]

The daily addition of 0·1 mgm. of copper (in the requisite amount of copper sulphate) or 0·1 mgm. of iron (in iron ammonium citrate) or both, to the food of rats for 10 days prior to their intraperitoneal inoculation with blood from a *Trypanosoma lewisi* infected rat will raise the resistance to such an extent that in 50 per cent. of the animals the infection is completely aborted. Lead, when tested in the same way, had no beneficial effect. Young rats brought up on a diet entirely free from copper or iron were not favourable subjects for the development of this trypanosome. *C. M. Wenyon.*

SCHWETZ (J.). L'influence de la splénectomie sur l'évolution de *Trypanosoma lewisi*. [**Influence of Splenectomy on the Development of *T. lewisi*.**]—*Bull. Soc. Path. Exot.* 1934. Jan. 10. Vol. 27. No. 1. pp. 62–70

Experimenting with a number of rats the author has found that splenectomy has little if any influence on the course of a *Trypanosoma lewisi* infection. It was not found possible to infect splenectomized mice with this trypanosome. *C. M. W.*

GALLIARD (H.). Les formes de multiplication de *Trypanosoma duttoni* Thiroux, au cours d'infections mortelles chez la souris. [**Multiplication Forms of *T. duttoni* in Fatal Infections in Mice.**]—*Ann. Parasit. Humaine et Comparée.* 1934. July 1. Vol. 12. No. 4. pp. 273–277. With 2 figs. [13 refs.]

The author has noted that the inoculation of mice already infected with a strain of *Trypanosoma gambiense* of low virulence with the natural mouse trypanosome, *T. duttoni*, may lead to an intense and fatal infection of the latter, during which large numbers of reproducing trypanosomes, like those of *T. lewisi* in the rat, appear in the blood. Normally *T. duttoni* produces a mild infection in mice, which always recover. Conversely the inoculation of mice already infected with *T. duttoni* with the strain of *T. gambiense* leads to an increased virulence of the latter, producing death in 35 to 38 days. Mice infected with the strain of *T. gambiense* alone survived many months. *C. M. W.*

LASSABLIÈRE (P.) & PEYCELON (A.). Exaltation de la virulence du *Trypanosoma gambiense*. [**Exaltation of the Virulence of *T. gambiense*.**]—*Rev. Méd. et Hyg. Trop.* 1934. May–June. Vol. 26. No. 3. pp. 138–139.

It is recorded that a strain of *T. gambiense* maintained in guineapigs increased in virulence so as to kill them in 9 to 12 days instead of in 3 or 4 weeks as previously. *W. Y.*

REINER (L.) & SMYTHE (C. V.). **Glucose Metabolism of the *Trypanosoma equiperdum* in Vitro.**—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1086–1088.

Experiments were undertaken to estimate the amount of glucose and oxygen consumed by trypanosomes *in vitro* and to ascertain the products formed aerobically and anaerobically. The paper is of a technical nature and should be consulted in the original by those interested. *W. Y.*

Schilling (Claus), with H. Schreck, H. Neumann, & H. Kunert. Versuche zur Schutzimpfung gegen Tsetsekrankheit. I. Teil. [**Experiments on Protective Inoculation against Tsetse Diseases.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Aug. 15. Vol. 83. No. 1/2. pp. 71–94. With 6 figs.

This paper, which apparently was submitted for publication in September, 1933, appears to be very similar to those published after this date in several other journals—English, French and German [this *Bulletin*, Vol. 31, p. 213 and p. 586]. Once more we are given detailed accounts of the foals, " Zeus," " Lottchen " and " Erna " ; and these are followed by a theoretical discussion. *W. Y.*

Schilling (S. Claus), assisted by H. Schreck, H. Neumann & H. Kunert. **Immunisation against Trypanosomiasis.**—*East African Med. Jl.* 1934. June. Vol. 11. No. 3. pp. 83–88.

This paper is substantially the same as one previously published by these authors [this *Bulletin*, Vol. 31, p. 213 ; p. 586]. *W. Y.*

Nattan-Larrier (L.). Longévité des cultures de *Trypanosoma rabinowitchi*. [**Longevity of Cultures of** *T. rabinowitchi*.]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 25. pp. 922–924.

The author describes how a culture of *Trypanosoma rabinowitchi* of the hamster on N.N.N. medium prepared with rats' blood was still alive after being kept at 22°C. for 403 days. *C. M. W.*

Komiya (Shoji) & Fujibayashi (Michizo). Beitrag zur Rieckenberg's Reaktion. (Ueber das Trypanolysephänomen.)—*Fukuoka Acta Med.* (*Fukuoka-Ikwadaigaku-Zasshi*). 1934. Oct. Vol. 27. No. 10. [In Japanese pp. 2365–2370. German summary p. 124.]

Moroder (Juan). Enfermedad del sueño. Resumen de las publicaciones aparecidas en los ultimos cinco años. Prólogo del Prof. Gustavo Pittaluga. —82 pp. [360 refs.]

Paris Eguilaz (H.) Contribucion al estudio de los sindromes neurologicos en la trypanosomiasis humana.—*Medicina Paises Cálidos*. Madrid. 1934. Aug. Vol. 7. No. 8. pp. 362–369.

Steudel (E.). Wie bewährt sich Bayer 205 als Heilmittel gegen die Schlafkrankheit? Nachtrag zu dem gleichnamigen Artikel in Nr. 51, S.2009, Jahrg. 1933 ds. Wschr.—*Muench. Med. Woch.* 1934. Aug. 10. Vol. 81. No. 32. pp. 1235–1236.

Torrealba (J. F.). Algo mas sobre tripanosomosis ensayos de xenodiagnostico. —*Gac. Med. de Caracas*. 1934. Feb. 15. Vol. 41. No. 3. pp. 33–37.

Universidad Buenos Aires Misión de Estudios de Patología Regional Argentina Jujuy. 1934. Publicación No. 15. pp. 1–24. With 15 figs. [21 refs.] Investigaciones sobre la enfermedad de Chagas. I. Sobre nódulos de histiocitosis en el Higado de perro inoculado con *Schizotrypanum cruzi* Chagas, de origen humano [Mazza (Salvador) & Jorg (M.E.)].

Universidad Buenos Aires Misión de Estudios de Patología Regional Argentina Jujuy. 1934. Publicación No. 15. pp. 25–54. With 1 chart & 33 figs. Investigaciones sobre la enfermedad de Chagas. II. Otro caso de forma aguda de enfermedad de Chagas observado en el norte santafecino [Mazza (Salvador) & Romaña (Cecilio)].

SPRUE.

MACKIE (Thomas T.). **Nontropical Sprue.**—Reprinted from *Med. Clinics North America.* 1933. Vol. 17. pp. 165–184. With 2 figs. [61 refs.]

This article, though entitled Non-tropical Sprue, starts by giving an excellent and well-balanced account of the condition as it occurs in tropical countries and is one of the best short summaries of our present state of knowledge the reviewer has read for a long time. Due credit is given to all those who have made a name in this field of research; their views are stated fairly and criticized without bias.

In the latter half of the article the author details a case presenting all the characteristic features of sprue, the patient, a woman of 43 years, having lived practically all her life in New Jersey, and never having visited a country where sprue is endemic. There is no need here to describe in detail the symptoms; the case was obviously one of severe grade and all the usual modes of treatment were adopted. It affords another example of the value of intensive liver therapy, administered parenterally, and at the same time shows that intravenously it may induce a rapid fall in blood values.

The article ends with a very good bibliography, the only omission of note being reference to the larger work, the book by Professor THAYSEN on this subject (see this *Bulletin*, Vol. 30, p. 57). Smaller papers by the same author are mentioned. This book perhaps has not come to Dr. Mackie's notice for in his list of cases of non-tropical sprue, which he regards as comprehensive, there are some not given which are mentioned in Professor THAYSEN'S work, *e.g.*, some of the cases recorded in Norway, Denmark, Germany and Switzerland. Dr. Mackie and his collaborator, Miss HENRIQUES, have done good service in putting this vexed subject so clearly and succinctly before us.

H. H. S.

THORFINN (Einar). **A Contribution to the Knowledge of Native Sprue in Sweden.**—*Acta Med. Scandinavica.* 1933. Vol. 80. No. 4–6. pp. 389–402. With 2 figs.

The case detailed in this article is the third indigenous in Sweden, possibly the fourth but there was a little doubt concerning one recorded by ENGEL in 1931.

The present patient was a woman of 36 years who had exhibited certain sprue-like symptoms on and off for 10 years. The clinical condition need not be detailed, for it was very typical—languor, debility, dry wrinkled skin, loss of weight, some anaemia, low blood pressure, low blood calcium, copious, frothy grey stools; the tongue was not affected till later. Results of physical and laboratory examinations are stated [enumeration of tests by mere names is to be deprecated; thus very little information is conveyed by the statements: urine Schlesinger negative; faeces Schlesinger highly positive, Weber negative, Schmidt positive].

Interest lies in the facts that blood transfusion was needed, and that diet and the administration of calcium were practically ineffectual till tabloids of parathyroid were also given. The patient left hospital much improved; she had gained 2·2 kgm. in weight, the stools were solid, but still contained more than the normal amount of fat. A

month later a relapse began and she was again admitted to hospital where she remained for nearly 8 weeks; she was treated by hydrochloric acid, calcium and vigantol and a diet "rich in protein and carbohydrate and with as little fat as possible." Improvement was less marked than on the first occasion and when seen two months later the stools were still light in colour, occasionally loose and there had been some stomatitis, but there had been a slight increase in weight and "the general condition was rather good." No parathyroid was given on the second admission to hospital and the diet "rich in carbohydrate" is against the most modern treatment. [The references given are all Scandinavian; no mention is made of the work of FAIRLEY and others in Great Britain.] *H. H. S.*

MILLER (Reginald). **Sprue commencing at 11½ Years of Age.**—*Proc. Roy. Soc. Med.* 1933. Dec. Vol. 27. No. 2. pp. 113–115 (Sect. for Study of Dis. in Children pp. 1–3). Also in *Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. pp. 413–416.

The most noteworthy feature of the case here recorded is the age of the patient. Generally speaking sprue is a disease of adults; though instances of adolescents are recorded they are very uncommon, and, so far as the reviewer is aware, none have been reported so young as this, 11½ years. Apart from this, the case—the history, clinical condition, response to treatment—is a typical one. The child lived from the age of 5 to 11 years in Ceylon, developed gastro-intestinal symptoms six months after returning to England and stomatitis six months later. There were wasting, fatty, copious, pale stools and anaemia (r.b.c. 1,400,000; Hb. 36 per cent., C.I. 1·3) of megalocytic type (8–8·5 μ). Treatment with high protein, low fat and low carbohydrate diet and liver extract led, as usual, to marked improvement.

H. H. S.

LOW (G. Carmichael) & FAIRLEY (N. Hamilton). **Fatal Perforation of the Caecum in a Case of Sprue.**—*Brit. Med. Jl.* 1934. Oct. 13. pp. 678–679. With 1 chart.

Perforation of a sprue lesion in the large intestine must be of rare occurrence. All the previous records in the literature to which the authors refer were of perforations of ulcers in the small intestine.

The patient, a woman of 58 years, had lived for a quarter of a century in India and during the first 2 years of her residence there had suffered from malaria and dysentery. Sprue symptoms first made their appearance in the last year of her stay in India; these symptoms were typical, together with considerable anaemia of the megalocytic type—r.b.c. 1,700,000 per cmm., Hb. 50 per cent., C.I. 1·4, average corpuscle diameter 8·6 μ. Serum calcium was down to 8·7 mgm. per 100 cc. On a treatment with high protein, low fat and carbohydrate she made considerable progress. In 6½ weeks the r.b.c. were 3,585,000 per cmm., Hb. 50 per cent., C.I. 0·7. Two days later signs of perforation and peritonitis appeared suddenly, and at operation the site of the perforation was found "posteriorly, . . . at the junction of a mobile caecum and ascending colon some two-and-a-half inches above the base of the appendix." The patient died. *H. H. S.*

MACKIE (F. P.) & FAIRLEY (N. Hamilton). **Gross and Microscopic Anatomy of the Intestinal Canal from Two Cases of Sprue.** [Laboratory Meeting Demonstration.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. p. 340.

The two specimens of intestine from sprue patients shown at the Clinical Laboratory meeting of the Royal Society of Tropical Medicine and Hygiene in November 1933 are of more than ordinary interest. In the first place the autopsy was performed so soon after death that post-mortem changes can be excluded. In the second place the hitherto recognized idea that an essential part of the morbid anatomy of this disease is a thinning of the bowel " to such an extent as to be almost diaphanous " is shown not to hold good for all cases and since examination rarely (if ever before) has been made so early after death, we are led to wonder whether this is not in great degree, perhaps entirely, a post-mortem change, for in neither of those exhibited on this occasion was any thinning found, or any other macroscopic morbid change except congestion of the margins of the valvulae conniventes. Moreover, microscopical examination also revealed no change of importance. *H. H. S.*

RHOADS (C. P.) & CASTLE (W. B.). **The Pathology of the Bone Marrow in Sprue Anemia.**—*Amer. Jl. Path.* 1933. Vol. 9. No. 54. Supp. pp. 813–826. With 6 figs. on 3 plates. [13 refs.]

Describes the marrow changes occurring in sprue and suggests an explanation of the variations in results previously recorded.

The somewhat divergent results of examinations of bone marrow in sprue, as recorded by MACKIE & FAIRLEY, KRJUKOFF, ASHFORD, and others, are ascribable to two chief causes : first, some specimens were taken in life, others after death ; second, the specimens studied were not always from comparable sites. The sternal marrow may reveal changes when that of the long bones shows none.

This article is based almost entirely on specimens of marrow from the sternum (in three from the femur also). Twenty-two patients were studied ; sixteen were untreated cases, five treated, and in three the examinations were made after death. In some the samples were taken both before and after a remission and in others during the height of reticulocyte response to liver therapy. The results are presented fully in tabular form ; this table should be studied in detail. A few remarks may here be made on illustrative cases.

1. A Porto Rican woman of 47 years, with typical sprue of one year's duration. The bone marrow was moderately cellular and treatment with liver extract even in large doses led neither to reticulocyte rise nor to improvement in the blood. Both, however, were satisfactorily accomplished when iron (Ferri et ammon. cit.) was given.

2. A man of 60 years, with sprue symptoms for ten years. Before the specimen of marrow was taken he was given Ferri et ammon. cit. 6 gm. daily for 10 days without effect. Liver extract *per os* was followed by a slight rise in reticulocytes but the normal was not attained till after parenteral administration.

3. A Porto Rican woman of 60 years ; sprue symptoms for a year. The marrow showed diffuse megaloblastic hyperplasia, similar to that of pernicious anaemia. Restoration to normal resulted from intramuscular injection of liver extract.

In two instances sternal puncture was performed at different stages and the histological pictures compared. One case is presented in detail together with photomicrographs to illustrate the differences, which are very considerable. The effect of the liver treatment was to bring about a maturation of megaloblasts to normoblasts and produce a bone marrow approaching the normal and resembling the transition observed in pernicious anaemia in course of treatment.

The post-mortem specimens resembled those found in patients dying of pernicious anaemia ; large marrow cells contained erythrocytes, the cells varied much in size and shape, some being very large and irregular with basophilic cytoplasm and containing many red corpuscles. Since this phagocytosis of erythrocytes was observed in post-mortem specimens only, the authors conclude that it is a post-mortem change.

They find that the alterations accompanying the anaemia of sprue are similar to those of pernicious anaemia ; that the anaemia of relapse results from the inability of the megaloblasts to form mature red corpuscles. The same fundamental change was observed in all the untreated cases—increase in number and size of megaloblasts, decrease in the fat, in number of megakaryocytes and cells of the granulocytic series. These changes found in sternal marrow may not be present in that of the long bones. During relapse the essential changes are proliferation of megaloblasts and reduction, even suppression, of maturation to the normoblast stage, restoration occurring when clinical remission takes place. [An article important for all engaged in pathological research on sprue. The photographs are well reproduced, but uncoloured they do not convey much information except when the differences are marked as in Figs. 4 and 5 depicting the marrow taken at different times from the same patient.] *H. H. S.*

Blanc (F.) & Bordes (L. A.). A propos du traitement de la sprue. [**The Treatment of Sprue.**]—*Marseille-Méd.* 1934. Feb. 25. Vol. 71. No. 6. pp. 297–301.

The authors' views are that, granting that the pathogeny of sprue is not yet fully clear, " we can at least explain the various symptoms of sprue as arising from a primary functional disturbance—a defect in the functions of the intestinal mucosa."

Their treatment consists in giving such form of nourishment as can be absorbed by a defective mucous membrane, namely the different sugars, hexoses and pentoses, glucose, laevulose, arabinose, in the form of fruit cooked or raw ; in addition raw meat (beef, mutton and horseflesh " whose absorption is facilitated by pepsin powder "). Further they give daily a shot-gun endocrine prescription containing pepsin, pancreatin, thyroid extract, insulin and adrenalin. Though they have not met with calcium deficiency " nevertheless we give calcium salts." Some patients, they state, take raw calves' liver with difficulty ! No cases are detailed and no comment is needed.

H. H. S.

RHOADS (C. P.) & MILLER (D. K.). **Intensive Liver Extract Therapy of Sprue.**—*Jl. Amer. Med. Assoc.* 1934. Aug. 11. Vol. 103. No. 6. pp. 387–391. With 4 charts. [14 refs.]

Examination of the various forms of dietetic treatment which have from time to time been recommended for and found successful in sprue has convinced the authors that the single factor common to all is a relatively high content of water-soluble vitamins. From this it is argued first that a lack of this vitamin exists in certain cases of the disease and, second, that this lack is "perhaps causal." [Neither of these points is anyone who has studied this disease likely to dispute.] The authors also state that "sprue may result from surgical intervention with the absorbing surface of the bowel." It is true that certain sprue-like symptoms may result from interference with absorption, but one would like more confirmation that surgical sprue exists.

Four cases are related briefly, patients who had not reacted effectively to ordinary modes of treatment, but improved greatly after intensive liver treatment administered parenterally—intramuscular injections of extract-Lilly, or the Parke, Davis & Co.'s preparation for intravenous use. [No reference is made to the large amount of research on sprue carried out by English workers in recent years.]

H. H. S.

RIEDER (Wilhelm). Erfahrungen bei der Behandlung einer Sprue-Tetanie mit A.T. 10. [**Treatment of Sprue Tetany with A.T. 10.**] —*Muench. Med. Woch.* 1934. Oct. 19. Vol. 81. No. 42. pp. 1610–1611. With 1 fig.

A.T. 10 is a preparation by Holtz, and was recommended by the author last year as *the* treatment for post-operative tetany. [Its composition is not stated.] He has now tried it in a case of sprue of long standing with excellent result after failure of other measures.

The patient had been under treatment of one kind or another almost uninterruptedly since 1919, and finally in 1932 came under the care of Professor GRIESBACH in Hamburg. With pancreon and parathormone he improved for a time, and the same results succeeded the administration of parathyroid. In January, 1934, he complained of lassitude, incapacity for work, and cramps in the hands and feet with tetany, as observed by the author to whose care the patient had been transferred, and stools of a fatty, sprue-like character numbered 15–20 a day. Blood pressure was low 100/65 ; calcium 4·8 mgm. per cent. (it had been as low as 3·5 in 1932). A.T. 10 was given [dose not stated here, but in later treatment it was given in doses of "2·5–3 cc. average "] and in a fortnight the blood calcium rose to 9·7 mgm. and in 4 weeks the stools were reduced to 5 a day. At the end of March, after another week's treatment with A.T. 10, the calcium was 10·5 mgm. per cent., but the number of stools did not diminish further. From the middle of April the drug was continued but in combination with raw apples, 8–10 daily, and the stools were reduced to one or at most two daily. Since then [the paper is not dated but the graph continues to June when presumably he left hospital to resume work] he has remained well, "feels himself equal to any demand that his occupation [not mentioned] makes upon him and states that he is the happiest man in the world." *H. H. S.*

Thaysen (Th. E. Hess). To Tilfaelde af idiopatisk Steatorré. Med saerligt Henblik paa Diagnosen og Forekomsten af Symptomer paa Endocrinopathi og Avitaminose. [**Two Cases of Idiopathic Steatorrhoea. Were the Symptoms due to Endocrine Disease or to an Avitaminosis ?**]—*Hospitalstidende.* 1934. Sept. 25. Vol. 77. No. 39. pp. 1033–1052. With 8 figs. (2 coloured on plate.)

Several papers have been published in Denmark on idiopathic steatorrhoea, and all have appeared in the period 1924–32. Evidently it is not very rare, and it is the more important for being readily overlooked and given some misleading label. The histories of Hess Thaysen's two patients (a man of 32 and a woman of 24) have this, among many other things, in common that they spent years in receiving hospital treatment as varied as the mistaken diagnoses. In the man's case, some of these diagnoses were gastric achylia, severe simple anaemia, haemolytic anaemia, chronic diarrhoea, pleuritis, tuberculous enteritis, renal tuberculosis, tuberculous epididymitis, tuberculous adenitis, heart disease, pulmonary tuberculosis, hypoadrenalism, megacolon, Addison's disease, and pluri-glandular insufficiency. The list of previous diagnoses in the woman's case was almost equally long and varied, and it included infantilism. It may be noted that in both cases Addison's disease was diagnosed on the strength of pigmentation. Since early childhood the second patient had been subject to periodic attacks of diarrhoea, with bulky, thin, foul, whitish or grey stools. Her build was definitely infantile, and she had a distended abdomen, though she was in other respects lean. Simple anaemia, glossitis, a low blood-sugar curve, increased basal metabolism, osteoporosis and latent tetany were observed in her case. After discussing the alternative diagnoses of endocrine disease and vitamin deficiency, and pointing out how many of the patients' symptoms could be correlated with one or other of these conditions, the author comes back to the problem of diagnosis. During one or more of their many stays in hospital, these patients must have passed the stools characteristic of steatorrhoea. It was, presumably, overlooked because of the quasi-universal hospital practice of consigning to nurses the duty of inspecting and passing judgment on stools. [See this *Bulletin*, Vol. 30, p. 57.] *C. Lillingston.*

Dünner (L.), Hirschfeld (H.) & Geraldy (M.). Zur Pathogenese und Klinik der nichttropischen Sprue (Fettresorptionskrankheit).—*Klin. Woch.* 1934. Jan. 27. Vol. 13. No. 4. pp. 138–141. With 1 fig.

Snijders (E. P.). Over Tropische spruw.—*Nederl. Tijdschr. v. Geneesk.* 1934. Sept. 22. Vol. 78. No. 38. pp. 4276–4285. With 6 figs. (3 on 1 plate).

van den Bergh (A. A. Hijmans). Een op spruw gelijkend ziektebeeld.—*Nederl. Tijdschr. v. Geneesk.* 1934. June 9. Vol. 78. No. 23. pp. 2559–2564.

YAWS AND SYPHILIS.

TURNER (Thomas B.), SAUNDERS (George M.) & JOHNSTON (H. M.), Jr. **Report of the Jamaica Yaws Commission for 1932.**—28 pp. With 66 figs. on 14 plates & 12 charts. 1934. Kingston: Govt. Printing Office.

At the request of the Government of Jamaica, the International Health Division of the Rockefeller Foundation agreed to undertake, on a co-operative basis, an investigation of yaws in the hope of devising more effective means of control. Thereupon the Jamaica Yaws Commission was organized and began to function in January 1932.

The present report is the result of the first year's work, and includes some general considerations upon the area selected for study, the method of survey to be carried out and some preliminary clinical observations based upon the first 1,500 cases admitted to the clinic. It may be stated at once that there is little essentially new to record but the observations of the commission are useful as confirmatory evidence upon certain points. The 1,500 cases studied comprised :—

	Per cent.
Yaws	917 or 61·1
Probably syphilis	15 ,, 1·0
No history : positive serology	113 ,, 7·5
No history : equivocal serology	30 ,, 2·0
No history : negative serology	425 ,, 28·3 [not 38·3]

91 per cent. of infections were acquired before the age of 15.

The primary yaw only differs slightly from the generalized yaw in appearance but tends to be larger. Many primary lesions are probably so insignificant as to escape notice. Enlargement of regional lymphatic glands is constant. *Sp. pertenuis* was demonstrated in the regional lymph nodes in two instances [it is not stated whether these were the only attempts made or not ; it would have been of value if similar examinations had been carried out in a large series]. " It would appear that dissemination of the organism by way of the lymphatics occurs before, and possibly as a necessary prelude to, the bloodstream dissemination which takes place eventually " [evidence on this point is sorely needed, the above statement would appear to rest on the findings in a single case]. " Despite the wide dissemination of virus which must occur, recognizable pathological changes are not often induced in any tissue save the skin and the bones." Among the 1,500 patients were eight presenting various [but undescribed] neurological lesions and with one exception a history of past yaws. The spinal fluid was definitely positive in 2, equivocal in 4 and negative in 2. The report states " The available evidence indicates that yaws probably gives rise to neurological disease in rare instances although it is desirable to have observations on a larger number of patients before making a final appraisal of the question." [It is certainly to be hoped that opportunity will arise of obtaining proof one way or the other and that " probables " will be discarded.] The evidence so far obtained in regard to cardiovascular lesions is of the same order.

A finding which must have considerable interest is stated thus :—

" Three patients presented lesions of the testis or epididymis which can be ascribed to yaws.

" Case 16.—Aged 9 years ; duration of infection 18 months, one previous treatment. Numerous skin lesions of the ' late ' type. Left testis twice size of right, lower half occupied by hard nodule.

" Case 563.—Aged 5 years ; duration of infection 1 month ; multiple dark-field positive framboesiform lesions and multiple bone lesions. Left testis enlarged, firm, irregular, painless.

" Case 1176.—Aged 2 years ; duration of infection 1 month, primary and generalized skin lesions dark-field positive. Multiple bone lesions, right testis enlarged to twice its normal size, firm, irregular, painless. In the epididymis were several small nodules strikingly like those which occur in the rabbit's epididymis in experimental yaws."

[From these notes it is doubtful what is meant by the phrase above given " which can be ascribed to yaws." Will they be *proved* to be definitely due to yaws and not merely left as cases of testicular enlargements in yaws subjects ?] " No instance of iritis or keratitis has been seen." " No lesion of the liver attributable to yaws was observed." All the well-known framboesial affections of the skin have been noted including plantar and palmar affections. " Involvement of mucous membranes alone in yaws is exceedingly rare . . . Papules lying wholly upon the mucous membrane surface . . . suggest direct inoculation." No true lesions of mucous membranes were seen.

The common well-known bone and joint lesions were met with, as in yaws elsewhere, in from 15–20 per cent. Several attempts to demonstrate the spirochaete in material obtained from bone lesions failed. The frequency of bone lesions demonstrable by X-ray was : tibia 39 : fibula 16 : ulna 18 : radius 14 : humerus 13 : femur 5 : carpal and metacarpal 14 : tarsal and metatarsal 3 : skull 2 : nose 3 : patella 1. Total cases 65. [Information is wanted upon the pathological changes in bone, the histological picture and the distribution of the organisms.] Seven patients presented characteristic juxta-articular nodules. All gave positive W.R. No history of yaws in three and a differential diagnosis could not be made. Two cases of goundou were seen—one a girl aged 12 with yaws of 9 years' duration, and multiple bone and late skin lesions, the other a man of 67 with yaws of about 60 years' duration, positive W.R. but no other lesions. Gangosa not infrequent but only one case admitted to the clinic. It was noted that " among our entire group of patients with generalized skin lesions there has not been one in which the rash, when viewed as a whole, would be confused by a qualified observer with that of syphilis."

Some of the results in attempts to evaluate treatment are as follows : The serological reaction in over 50 per cent. of cases treated by six injections of some one of the well-tried drugs is positive when tested 6–9 months after treatment. Lesions heal most readily after treatment with neo-arsphenamine but this arsenical is followed with just as bad a serological relapse rate as any other. With halarsol results are uncertain—further investigation is necessary. With bismuth preparations persisting infections are commoner than with the arsenical. Neo-bismuth preparations offer better results. Carbarsone deserves further trial.

No pathological work nor animal experimental research has yet been carried out. [The histo-pathological changes in yaws certainly need study afresh.]

Finally, the authors of the Report say " Whatever was the relation of yaws and syphilis one century or four centuries ago, it can be said

that at the present time the two diseases are not identical. . . . Advantage should be taken of the opportunity to study the two diseases concurrently."

[May we hope this Commission will do so. All those interested in the problem await "a sign from heaven," some acid test in differential diagnosis.] *H. S. Stannus.*

PURCELL (F. W.). **Aetiology of Yaws.**—*West African Med. Jl.* 1933. Oct. Vol. 7. No. 2. pp. 96–97.

In this article the author relates his observations upon some 5,000 cases of yaws, treated in 1928, among a single isolated tribe—the Konkomba—of the Eastern Dagomba District of the Northern Territories of the Gold Coast. They are offered as a contribution to the aetiology of the yaws–syphilis problem.

The Konkomba are an aloof people who do not marry into other tribes nor have other relations with them. No venereally contracted diseases, including gonorrhoea, occur among these people. Syphilis, acquired or congenital, as ordinarily diagnosed clinically is never seen. On the other hand a large proportion become infected with yaws, generally in childhood, among the uncleanly more especially. Reinfection, it is stated, may occur. The primary lesion in children is usually found on areas of skin exposed to contamination with the ground or exposed to injury by the finger-nails—the anus, the prepuce, the corners of the mouth and eye, etc.

The author is unable to entertain the idea that "yaws is epidemic non-venereal syphilis transmitted innocently among primitive people."

H. S. S.

BURKE (H. L.). **Some Notes on the Aetiology, Symptomatology and Treatment of Yaws in North-Eastern Adamawa Province, Nigeria.** —*West African Med. Jl.* 1933. Oct. Vol. 7. No. 2. pp. 94–96.

A study of 580 cases of yaws from the north-eastern portion of Adamawa Province of Nigeria and the adjacent area of British Cameroons, at the Lassa Hospital of the Church of the Brethren Mission.

It is noted that the Moslem population (Fulani) had no word for yaws while the pagan tribes had no word for syphilis, yaws being very rare among the Fulani and syphilis equally exceptional among the pagan peoples. [Illustrating again the well-known fact that yaws tends to be a disease of the less civilized who live in the bush while syphilis tends to occur among the more civilized living in communities.] "With a little experience the difference between yaws and syphilis is quite apparent."

Cases of primary yaws (36) seldom seek treatment; the majority of the sick (347) were in the stage of generalized eruption. The tertiary cases (101) most commonly presented lesions of the palms of the hands and soles of the feet, which had appeared 12–15 years after infection. Tibial periostitis, "prepatellar bursitis," "nodules of the sternum," "deformations of the skull," and gangosa are mentioned but there is no reference to the occurrence of juxta-articular nodules or goundou.

H. S. S.

Wilson (Paul W.). **Atypical Yaws.**—*Amer. Jl. Trop. Med.* 1934. Jan. Vol. 14. No. 1. pp. 1–25. With 19 figs.

A description of what are considered by the author to be atypical lesions met with during a study of 424 consecutive cases of yaws in Panama. A comparison is made between these cases and those of a series of 1,423 cases reported from Haiti. [See this *Bulletin*, Vol. 27, p. 708.]

Notes of twenty cases are given and the following conclusions drawn :—

" 1. The yaws cases seen in Panama show a marked tendency to local and regional limitation of late pathology [lesions].

" 2. Compared with yaws in Haiti, this regional limitation in the Panama series is double that found among the Haitien cases.

" 3. The route of transmission of infection from the primary yaw to other parts of the skin surface cannot be definitely traced in many instances but considerable evidence indicates an impetigo-like spread, *i.e.*, a mechanical transfer of infectious material over the body surface.

" 4. Undoubtedly transfer of the infection within the body is accomplished through the lymphatic system or general circulation in a small percentage of cases.

" 5. With but two exceptions all periosteal cases in the Panama group were caused by direct extension of the infection from overlying ulcers.

" 6. The strain of *T. pertenue* found in Panama is a much less virulent strain than that encountered in Haiti.

" 7. ' Dry yaws ' eruption, either of the ringworm or non-progressive papular type, probably accounts for the long quiescent periods so frequently seen in cases of late yaws.

" 8. ' Dry yaws ' on the skin around joint protuberances probably indicates the portal of infection which later manifests itself as a juxta articular node

" 9. It is believed that very rarely yaws may be the *accidental* etiological factor in aneurysm and cerebral thrombosis or cerebral hemorrhage of young adults." *H. S. S.*

Hewer (T. F.). **Some Observations on Yaws and Syphilis in the Southern Sudan.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. May 9. Vol. 27. No. 6. pp. 593–608. With 4 figs. on 1 plate.

The author had hoped to be able to make a comparative study of parallel series of cases of yaws and syphilis. His paper deals with observations made upon 250 cases of yaws and syphilis studied clinically and 1,000 others seen casually. He found himself unable to do more than place some proportion of his cases in one or other category of probably yaws or probably syphilis.

Many of the observations are very interesting though their value is uncertain as is always the case when they are correlated with histories depending on native information. As an example " *a history* of a primary on the genitals " can have little value without knowing definitely whether the primary was indeed a primary and then whether it was a primary syphilitic chancre or a primary yaw.

The reference to lesions on the mucous membranes are particularly interesting. Among 256 cases there are 62 with some lesion of the mucous membrane of the mouth or throat, of which 35 gave a history of sore throat and 21 of hoarseness in the early secondary stage ; 29 had mucous patches just inside the lips, 7 inside the cheeks. Of the 62 in

14 there was a history of a primary lesion on the genitals, 35 of an extra genital lesion, 13 were doubtful. Some of these had typical framboesia and crab yaws, many had genital condylomata and often no other manifestation. The author does not specifically aver that mucous patches occur in yaws but the inference is made and he offers as an explanation of this possibility the fact that the whole population chews tobacco and infants are given plugs of tobacco already chewed by their mothers.

No visceral lesions were discovered save a single case of aortic regurgitation attributable to syphilis.

In 246 cases the cerebrospinal fluid was examined, the standard of normality adopted being 3 cells and under, an upper limit of 30 mgm. total protein and negative Pandy test. The cases were divided into probably yaws, probably syphilis, and doubtful, and these again into three groups according to the duration of the disease. The yaws cases numbered 44 and among these " definite abnormalities were found " in five. It is worth noting, however, that the cell counts were $3\frac{2}{3}$, 7, $3\frac{2}{3}$, $6\frac{2}{3}$, $\frac{2}{3}$, figures which many syphilologists would pass as normal, the ranges in total protein 55, 30, 25, 20 and 50 mgm. per cent. The Pandy reaction was only done in two cases and in both it was positive. The author says, " in none of these cases was the change a gross one." In view of their numbers and lack of any series of controls and the fact that such changes are in no sense specific it seems questionable how they should be interpreted. It is a pity no W.R. were done on these fluids. No case of involvement of the nervous system was diagnosed clinically.

The facts given in regard to congenital transmission based on native evidence are too few and too uncertain to have much value.

H. S. S.

Le Scouézec. Syphilis avec réactions méningées et pian chez les indigènes du Caméroun. [**Syphilis with Meningeal Reactions and Yaws in Cameroon Natives.**]—*Arch. Inst. Prophylactique.* 1934. Apr.–June. Vol. 6. No. 2. pp. 186–190. English summary pp. 189–190.

The results of examination of the cerebrospinal fluid from cases of syphilis and yaws among natives of French Cameroon.

Of 3,045 fluids from syphilitics 1,412 or 46·37 per cent. were absolutely normal; 1,633 or 53·63 showed a more or less pathological deviation from normal using (1) Vernes-perethynol test, (2) hyperleucocytosis, (3) hyperalbuminosis as criteria. 7·6 per cent. showed (1)+(2)+(3); 22·9 per cent. (2)+(3); 23·7 per cent. (2) only; 45·8 per cent. (3) only.

The blood of 74 natives suffering from florid yaws, with the exception of two, showed sero-flocculation with Vernes-pyrethynol test. The C.S.F. of these 74 cases was normal except in 2 cases both of which showed positive flocculation (1) associated with (2)+(3); there were 9 in which (2) alone and 11 in which (3) alone was encountered.

Some of these fluids might be considered within the limits of normal by other observers and though these yaws cases showed no sign of syphilis and denied syphilis the author, very rightly, says he would not like to assert that these changes in the C.S.F. of yaws cases are due to yaws.

H. S. S.

Montel (M. L. R.), Massari (P.) & Le-van-Phung. Un cas de pian osseux tertiaire. [**Case of Tertiary Yaws : Bone Changes.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. May. Vol. 12. No. 5. pp. 477–482. With 4 figs.

A description of tertiary bony lesions with radiographic findings in a 15 year old Annamese boy.

The clinical picture calls for no special mention but the lesions shown by X-ray examination are worthy of note. They resembled those previously described by other authors and appear to have specific characteristics :—multiple and localized thickenings of the bones more especially the long bones, both epiphysis and diaphysis, the periosteum and bone both being involved, with obliteration of the medullary canal but preservation of the trabecular arrangement of the bony tissue. In these zones of thickening numerous rounded areas of rarefaction varying in size are seen always surrounded by a zone of more marked condensation. These areas of rarefaction sometimes involve the border of a bone and give rise to an appearance as if a piece of the bone had been bitten out. Between the areas of thickening a certain amount of decalcification may be seen.

In syphilis the lesions are less irregular, less numerous, and the medullary canal persists though with some degree of narrowing. In yaws the lesions in some ways rather resemble those seen in fibro-cystic disease of bone. *H. S. S.*

Fitzgerald (G. H.) & Gupta (Prafulla Kumar Das). **The Treatment of Yaws.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. pp. 371–384. [15 refs.]

An attempt to evaluate various methods of treatment in yaws. Local conditions in Assam demanded a method which was cheap, painless and free from danger and which could be administered by the needle.

The best results were obtained, the authors consider, with 2 or 3 injections of neosalvarsan (0·01 gm. per kg. body weight) combined with 8 injections of bismuth (1·5 gm. bismuth metal). Serological cure was obtained in half the cases and freedom from clinical relapse in all but 5 per cent. This course involved 8 weekly attendances and was possible in the area under observation but one which might not be possible in other yaws districts.

Neosalvarsan or one of its substitutes alone failed ; 80 per cent. of cases treated by 1 to 3 injections were either clinically or serologically positive two years after treatment.

A number of bismuth preparations were tried out ; that which appeared to have greatest advantages was " Casbis." Given alone like other bismuth salts, it was of little value in effecting persistently good results but in combination with the arsenical as above mentioned it was the most useful.

Halarsol has practically no value alone ; combined with bismuth it is more effective. Notes of trials with other drugs are given but in no case were useful results obtained. *H. S. S.*

Occhino (A) & Kernkamp (Y.). Le traitement de quelques affections et notamment du pian par les injections intraveineuses de sulfate de cuivre. [**Treatment of Yaws by Intravenous Injections of Copper Sulphate.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. Dec. 31. Vol. 13. No. 4. pp. 397–404. With 8 figs.

A short paper upon the uses of intravenous copper sulphate therapy in yaws and some other conditions, including impetigo, erysipelas and leprosy.

Secondary yaws cases to a total of 209 were selected for trial. The course of treatment consisted in the daily intravenous injection of a 6 per mille aqueous solution of copper sulphate ($Cu\,SO_4 \cdot 5\,H_2O$) in 10 cc. doses for adults and half that amount for children of 10 years of age. " Blanchissement " was obtained in from 10 to 25 days. A further 5 injections were given as " a treatment of consolidation." No relapse occurred in 193 of these cases which remained under observation for from 2 to 5 months.

These results the authors hold are comparable with those obtained with arsenic and bismuth. The one disadvantage is that the method entails *daily* treatment. The advantages are the ease of preparation, absence of unpleasant reactions and very low costs. Relief of pain is obtained early. [No serological reactions were carried out and with an observation period of only 2 to 5 months it is obviously uncertain how this form of treatment should be evaluated in regard to cure of the infection.] *H. S. S.*

Bais (W. J.). Ueber Behandlung der Framboesia tropica mittels Bisuprol. [**Treatment of Yaws by Bisuprol.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Mar. Vol. 38. No. 3. pp. 118–124.

The author finds bisuprol to be an efficient preparation of bismuth in the treatment of yaws.

Yaws is widespread among the child population around Medan in Sumatra. In the earlier trials (1931) this drug in emulsified form was given in 2 cc. doses every three days for adults. The following year it was found that single doses of 10 cc. of a 6 per cent. emulsion (=600 mgm. colloidal bismuth), half each side intragluteally, were as efficacious and were an advantage in the case of a population whose attendance for treatment was irregular. The effect of this depot method of treatment probably lasts over 4 weeks. The results in secondary and tertiary cases were rapidly obtained while primary lesions were more resistant. With the larger doses pain was more marked but not sufficient to prevent their use. A few children developed stomatitis and one a fairly severe dermatitis ; otherwise no unpleasant results were witnessed.

A certain number of patients were kept under observation by giving subsequent injections of saline, and it was in these that the excellent immediate results were noted. They were clinical results only. The ultimate results are unknown and no serological tests were carried out. *H. S. S.*

Galinier (Georges). La gangosa et les rhino-pharyngites mutilantes des tropiques. [**Gangosa and Rhinopharyngitis Mutilans of the Tropics.**]—87 pp. [127 refs.] 1934. Paris : Jouve & Cie, Éditeurs, 15 Rue Racine.

A Paris thesis embodying observations made upon a single case of gangosa in Indo-China together with a study of some of the literature

on this condition. In a number of short chapters the history, definition, distribution, pathogeny, symptomatology, diagnosis, etc., are dealt with. Without bringing to light any new facts this brochure will form a handy volume of reference.

The author believes gangosa to be a disease *sui generis*, of unknown causation and differentiates between this condition and those similar conditions due to yaws, syphilis and leishmaniasis which he would include under the term rhino-pharyngitis mutilans. *H. S. S.*

Tani (T.) & Ogiuti (K.). Weiteres ueber die Meerschweinchenframbösie. [**Yaws in Guineapigs.**]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Apr. 5. Vol. 131. No. 3/4. pp. 146–148.

A method of differentiating between the spirochaetes of yaws and syphilis by animal inoculation.

Kakishita showed that when an inoculum containing the " Manilla " strain spirochaete of yaws was injected into the testicle of the guineapig a metastasis appeared on the prepuce, and that infection into the preputium itself resulted in the production of a characteristic lesion which persisted for as long as 230 days. The authors have now repeated these experiments using a strain of yaws spirochaete from a Malay woman after three passages through rabbits. The spirochaete of yaws shows an affinity for the prepuce in contradistinction to the spirochaete of syphilis. *H. S. S.*

Turner (Thomas B.) & Chesney (Alan M.). **Experimental Yaws. II. Comparison of the Infection with Experimental Syphilis.**—*Bull. Johns Hopkins Hosp.* 1934. Mar. Vol. 54. No. 3. pp. 174–185.

In this second communication [see this *Bulletin*, Vol. 29, p. 723] the authors report the results to date of their experimental yaws infections in rabbits comparing them with experimental syphilis infections in the same animals, the strains of *S. pertenuis* and *S. pallida* all having been obtained from Haiti as the purpose of the investigation was to obtain and experiment with strains of spirochaetes from cases of yaws and from cases of syphilis *encountered in the same locality*.

The surviving strain of *S. pertenuis* is designated " Y 9 " and has been passed through 15 generations of rabbits. The strain of *S. pallida* is designated " strain K " and has been passed through 20 generations of rabbits.

In comparing the two infections in rabbits attention was focussed on (1) incubation period, (2) initial lesion after (*a*) intratesticular and (*b*) intracutaneous inoculation, (3) metastatic lesions, (4) seasonal variation.

Results went to show that no differences were noted in the experimental infection in rabbits inoculated with eight different strains of yaws virus. The disease picture produced by the yaws virus presented striking and for the most part constant differences from that produced by the Haiti strain of syphilis. The Haiti strain of syphilis gave rise to an experimental disease in rabbits which was similar in every way to that produced by several strains of syphilis virus isolated in the temperate zone. These results lend support to the view that yaws and syphilis are different diseases. *H. S. S.*

Fivoli (Filippo). La sifilide indigena in Tripolitania (aspetti e profilassi). [**Indigenous Syphilis in Tripolitania.**]—*Giorn. Ital. di Malat. Esot. e Trop.* 1934. June 30. Vol. 7. No 6. pp. 148–50, 153–6, 159–62, 165. With 6 figs.

A general account of syphilis as it occurs among the inhabitants of Tripolitania, the means adopted for its control and the results obtained.

In the Italian colonies of N. Africa syphilis is one of the principal causes of morbidity. It is more widely diffused towards the south and the interior than in the coastal regions and among the Arabs and coloured peoples than among the Jewish population, and the graver forms of the disease are associated with the higher incidence largely due to lack of resistance.

The disease as met with by Fivoli resembles that already described by others in similar populations. Among town dwellers it is contracted sexually but it is otherwise in the nomad peoples among whom ordinary hygienic measures and cleanliness are lacking, dermal parasitism is general and over-crowding the rule. Two special factors have also to be noted—prostitution and homosexual practices both among men and women. Patients seldom present themselves with primary lesions ; the primary sore when seen (and in the male only) does not differ from that seen in Europe. That marked primary lesions with secondary infections would be seen under the conditions of filth which exist might be expected, but their absence is explained by the practice of circumcision.

Well marked differentiation into secondary and tertiary periods in the evolution of the disease is seldom witnessed. Earlier roseolar and papular eruptions may go unnoticed so that papulo-squamous lesions are most commonly seen often undergoing pustular and ulcerative changes ; ecthyma and impetiginous lesions are common, and vitiligo is not uncommonly observed and of course not easily missed in darker skinned people. Associated lesions of the mucous membrane of the mouth and of the skin about the anus are general, the exciting factor for the former being, it is suggested, the use of hot condiments and excessive smoking. Gland enlargement is general but of no diagnostic value. Tertiary lesions often appear to overlap secondary lesions and frequently cannot be distinguished ; secondary lesions often appear to be transformed into tertiary lesions after they have existed some time.

The greatest havoc is wrought upon bones, joints and muscles and with equal frequency the eye may be attacked—iridocyclitis. Very rarely are the viscera affected and still more rarely the nervous system.

The greater part of the cases coming under observation have already reached the tertiary stage and present ulcerative nodular and sclerogummatous lesions of the skin, often very extensive and sometimes phagaedenic, together with gummatous lesions of palate and nose.

Abortion, premature birth and high infant mortality are considered to be due to syphilis. The commonest lesions in the congenital disease are snuffles, rhagades, keratitis, choroiditis, hydrocephalus, many dystrophies, infantilism, rickets, hare-lip, cleft palate and above all polydactylism, so common among these peoples [!] Many lesions of the inherited disease cannot be distinguished from those of the acquired disease. [Such a statement as it stands should I think be received with reserve ; many cases which might be considered as cases of inherited syphilis may in reality be cases of infantile infections. It is a question

constantly turning up in the consideration of native syphilis and remains unsettled.

In regard to the dystrophies mentioned above we see here reflected the ideas of the continental school. The reviewer would point out that many years ago writing upon congenital abnormalities in African natives (*Biometriña* 1914) it was shown how common they were, especially polydactylism, and this in a people among whom there was comparatively little syphilis.]

The anti-venereal measures adopted consisted in the regulation of prostitution and the provision of methods of inspection and treatment centres. This side of the question need not be further commented upon here. *H. S. S*

Boenjamin (R.). Een proef met solganal B bij salvarsan-resistente framboesia tropica.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Jan. 16. Vol. 74. No. 2. pp. 116–120.

MISCELLANEOUS.

LAMBERT (S. M.) **The Depopulation of Pacific Races.**—*Bernice P. Bishop Museum Special Publication 23.* 42 pp. With 11 figs. 1934. Honolulu, Hawaii. Published by the Museum. [Summary appears also in *Bulletin of Hygiene.*]

The paper discusses the effect of Europeans on native populations in Melanesia and Polynesia, and gives an account of the present state of these peoples.

The problem which Dr. Lambert has set himself to consider is fascinating in its complexity. The investigator must bear continually in mind that there are great differences in race, customs and outlook in different parts of Oceania. Furthermore, malaria is prevalent to the west of 170°E. but absent from Fiji and Polynesia, which lie to the east of that limit. Apart from this, the effects of European penetration have been extremely diverse, some of them greatly to our credit, others disgraceful. The trader, the missionary and the official had little enough in common, but they were equally effective in destroying much of the endemic social life ; but their effect varied with different archipelagos according to the European Power which possessed itself of the islands and the missionary society within whose zone of activity they chanced to fall. As the forces at work have been numerous and conflicting, it is not surprising that their effect has been dissimilar. Some islands, for instance the Samoan group, were never gravely depopulated : from others the people vanished fifty years ago, and in others again they are now disappearing. The field worker, especially in Melanesia, will frequently observe great differences even between islands which are close to one another and in which the people, climate and diseases appear to be similar.

Dr. Lambert's work gives a good general account of the problem, and shows that the state of most of the populations is more prosperous than many Europeans believe. Without going exhaustively into the matter, he introduces the reader to some early travellers and their estimate of populations; then passing to modern times, he sets out such statistics as may be available. In this way he reviews most of the island groups of Melanesia and Polynesia.

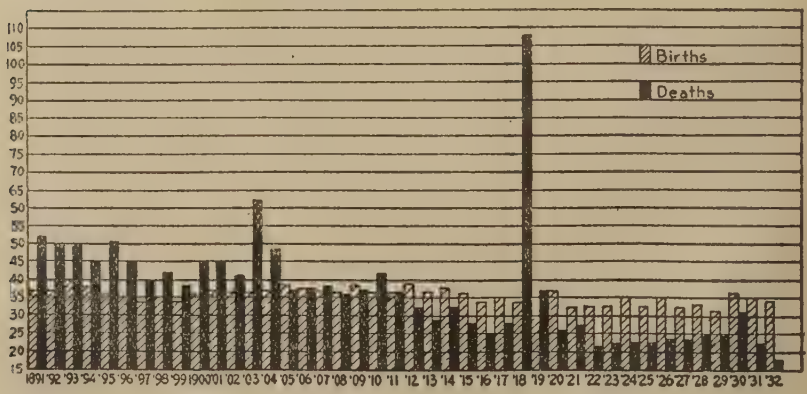


Fig. 1.—Native Fijian birth and death rates.
[Reproduced from *Bernice P. Bishop Museum Special Publication 23.*]

His treatment of Fiji may be considered here. It seems that births and deaths have been recorded in a trustworthy manner since 1891. The population at that time was 105,800 and it was declining (it was estimated at 300,000 in 1870). About 1905 the population, which had fallen to 87,000, became stationary, but since 1911 there has been a steady rise interrupted by the influenza in 1918. During the whole period since 1891 the births have been nearly stationary at about 35 per 1,000, but the deaths have fallen from 50 to 18 (fig. 1). The author's view is that this is due almost entirely to effective public health measures, and he mentions particularly campaigns against yaws, dysentery and hookworm. He rightly gives prominence to the work of the Native Medical Practitioners and to the importance of the Central Medical School at Suva, Fiji, which gives a solid practical course to suitable young men not only from Fiji but from other archipelagos. Within recent years infant welfare centres have been established in several parts of Fiji, and some at least of the reduction in mortality in the first five years of life is credited to them (fig. 2). The problem of Fiji is particularly complex, for the native race must not only adjust itself to Europeans but also to Indians, of whom large numbers have come in as indentured labour since 1881; but it seems clear that the adjustment has been made, and that the Fijian race is surviving.

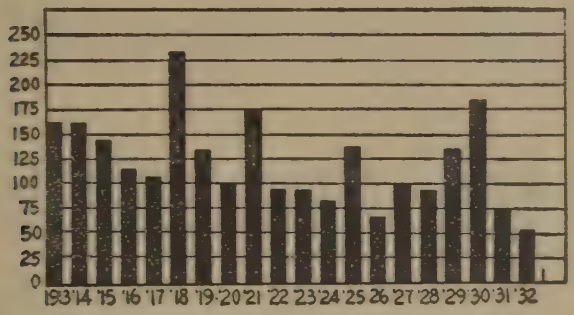


Fig. 2.—Fiji mortality of children 1 to 5 years of age.

[Reproduced from *Bernice P. Bishop Museum Special Publication 23.*]

Dr. Lambert's view may be summarized thus. There is no doubt that the depopulation was in some way caused by the white man. As to the causes we have little precise knowledge, but it is clear that introduced diseases were an important element. At the present moment the populations of most islands are stationary or rising. This may be due to a general adaptation to new life and introduced diseases, but it has clearly followed the introduction of preventive medicine, the direct effects of which are observable in a number of instances [the careful reader may discover for himself that the races which are still dying out are all administered under one flag, and that they receive less medical and sanitary help than the rest of Oceania].

As to the future and the grave menace of over-population of small islands, not a word is said. *P. A. Buxton.*

Lhérisson (Camille). La patología de los campesinos haitianos. [**Disease among the Rural Population of Haiti.**]—*Bol. Oficina Sanitaria Panamericana.* 1934. Sept. Vol. 13. No. 9. pp. 821–834. With 8 figs. [22 refs.] English summary.

Plague, typhus and relapsing fever appear to be unknown, but almost every other disease of the tropics is found in Haiti. Enteric fever is common; dysentery also, both the bacillary and amoebic varieties. The former (Flexner and Shiga) is epidemic and, each year, is said to attack about 25 per cent. of the people; the latter is more common in the northern districts, affecting from 10–20 per cent. of the inhabitants. *Balantidium coli* is also met with. Geophagy is frequent among the children. In 1925 among 4,439 persons examined in 3 districts, 30 per cent. had hookworm, 43 per cent. Ascaris, and 58 Trichuris. Goitre is common in the mountainous regions and pinta in the plains. Tuberculosis is very fatal and in the hospitals accounts for 30 per cent. of the deaths. Malaria is rife; of 4,439 examined by the Rockefeller Mission staff 67 per cent. had parasites in their blood and of 11,000 emigrating to Cuba to work in the fields of the United Fruit Company 23·5 per cent. were infected. Subtertian predominates and the vectors are *A. albimanus* and *A. grabhamii*. The commonest of all diseases, however, is yaws; of 2,564 examined in the environs of Port-au-Prince 78 per cent. were suffering and among 3,289 cases, 61·9 per cent. were children under 10 years. The article contains an illustration of the crippling effects of this disease.

A National Public Health Service was established in 1919 and "the peasant is becoming every day more conscious of the value of health," but much remains to be done. *H. H. S.*

Pascal (J. M.). Essai médical sur le Mzab (Sahara algérois). [**Mzab (Algerian Sahara) from the Medical Side.**]—*Arch. Inst. Pasteur d'Algérie.* 1934. Mar. Vol. 12. No. 1. pp. 83–167. With 33 figs. (23 on 15 plates). [Refs. in footnotes.]

A complete account of this region of the Sahara from the medical side—its soil, climate, hydrography, inhabitants, native medicine and diseases. This annotation concerns chiefly the last.

The Mzab, lying on the northern edge of the Sahara, is a rectangle comprised between the 2nd and 5th degrees of east longitude and 31·3° and 33° north latitude. Ghardaia, its capital, is 480 kilos, as the crow flies, to the south of Algiers. Here the author practised for seven years. The climate is saharan. There is a difference of 17 degrees between day and night and 50 degrees between summer and winter. Air humidity is very low. In the last ten years the average rainfall has been 62 mm. The inhabitants consist of 22,000 Mzabites, 16,000 Arabs and 1,500 Jews; the first are of Berber origin and are the traders of the district. The diseases met with are discussed in order of decreasing importance—

Conjunctivitis. These patients make up one-third of those seen at hospital and more than half in spring and autumn. A table shows that in 37 bacteriological examinations the diplobacillus of Morax was met with 17 times, the gonococcus 3 times and the bacillus of Weeks twice. Trachoma is almost universal. There are eye dispensaries in every

village of more than 500 inhabitants and they are visited by a doctor at least twice a month. Most of the work is done by infirmiers but they are insufficiently paid and patients attend very irregularly. Excellent work in preventing the sequelae of trachoma is done at the schools.

Syphilis. Of 226 men who came to hospital (some for the treatment of their syphilis), 68 had clinical signs of the disease and of 134 who appeared to be free and whose serum was examined (Wassermann and Meinicke) 14 were infected, a percentage in all of 37. Primary lesions were rarely seen but penial scars were less uncommon. Three cases of tabes were seen in Mzabites in the course of 3 years. Rickets characterized by late appearance of incisors, late acquisition of walking and late closure of fontanelle is believed to be of syphilitic origin It occurs in the Mzabites, Arabs and Jews in similar proportions to that of syphilis in those races.

Tuberculosis is manifested at consultation chiefly in the bones and glands. The author studied 2,334 persons by the cuti reaction (Parrot & Foley). For children between 1 and 15 years it varied between 42·5 in negroes and 49·7 in Arabs; for all ages it was 56·2, one of the highest indexes in the Sahara. The installation of a sanatorium is for reasons stated not practicable.

Typhus does not exist normally in the Mzab. It is suggested that inspection of arrivals from places where it has broken out should suffice for prophylaxis. Lousing centres are of limited utility because the natives do not care to entrust their families to foreign hands.

Enteric fever occurs sporadically and does not seem very harmful to the natives.

Diphtheria occurs sporadically, *scarlet fever* only when introduced.

Dysentery, rabies, plague, cholera, are unknown.

Tinea. One hundred scholars of each race were examined; there were found 20 trichophytic infections and 37 favus; only one case of favus was in Jewish children.

Helminthiasis. 80 per cent. of scholars harbour intestinal worms, the Jews less than the others. A full table records the data for each race. Ascaris is by far the most frequent, then come Trichocephalus, Oxyuris and lastly Hymenolepis. Of this last he remarks that there are no rats in the Mzab and that Hymenolepis eggs have not been found in mouse droppings. The gardens are manured with human dejecta which also soil the water supply.

Scorpion stings are common. Every summer one or two children under 8 die from this cause. The author has ceased to employ local treatment, having seen some deep burns caused by permanganate.

Of *bugs* he writes—The bug is an imported article . . . after its introduction the whole family seems to be suddenly attacked by a contagious disease with a rash—.

The only mosquitoes found by the author are *Culex pipiens* and *Theobaldia longeareolata*. Others have recorded *A. aegypti* at Ghardaia. Anopheles have never been recorded.

Leishmaniasis. Three cases of Oriental sore were seen in the spring of 1932 in children who had never left the Mzab.

Malaria occurs but always introduced from without. *A. G. B.*

KIRK (J. Balfour). **The Health Unit System as a Means of applying the Principles of Preventive Medicine in Rural Areas in the Tropics.** —*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. May 9. Vol. 27. No. 6. pp. 587–592. [Summary appears also in *Bulletin of Hygiene.*]

Dr. Balfour Kirk, in his introductory remarks, lays stress on the fact which is common knowledge, it is true, but one of great significance in the Colonies, that the medical branch of the services, dealing mainly with curative treatment, has come to be regarded as distinct from the sanitation branch, dealing with hygiene and prevention, and further that the latter, being largely administrative and intimately connected with rules and regulations, and with penalties for infringement, " has become associated with compulsion," and all the world over compulsion implies resistance.

The author, who can speak with authority as one who has had considerable tropical experience, then states his conception of a rural Health Unit which has justified itself in Mauritius at least. This unit comprises a Dispenser, a Sanitary Inspector, a Health Visitor and a Midwife, and at the head a physician known as a Health Officer, who also is given the statutory powers of the Health Authority of his area. The duties of each are detailed and it is seen that, though there is the necessary cleavage between preventive and curative medicine proper, this is not so conspicuous because it occurs in the lower grades, in the subordinate staff. On epidemiological grounds (for example the early knowledge of something wrong or the beginning of an outbreak) this method is ideal in enabling prompt action to be taken.

Such a scheme would be particularly suitable in many, one might say most, of the tropical Colonies where the District Medical Officer is in charge of the local hospital and also acts as Medical Officer of Health of his district. This system moreover has the advantage of being capable of almost indefinite expansion without losing its essential characteristics. To those who have practised in the tropics the resistance—passive often, active sometimes—to any innovation is a matter of daily experience.

In an abstract one can do little more than point out the general trend of this valuable paper which should be read in its entirety and studied by all those practising in rural areas in the tropics. *H. H. S.*

MCKINLEY (Earl B.). **The Development of Tropical Medicine in the United States.**—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 299–307.

" Science " writes Dr. Earl McKinley, " has already learned more and has placed in the record more proven knowledge than the social and economic status of most tropical countries will permit of application." At the root of this failure to apply knowledge is poverty, for the methods of preventing disease must be of such low cost that the people can pay for them. He would have application of knowledge and search for new knowledge going on together, for only through continued research is progress made. He gives some account of the preliminary survey of tropical diseases which a committee of the U.S. National Research Council is carrying on. An attempt is being made to define the problem of disease in the tropical belt, *i.e.*, where certain diseases are prevalent, to what extent and with what distribution, and

enquiry is afoot as to what facilities are available for teaching and research. It is believed that when the problem has been defined both basic industries and private philanthropists will finance a public health program in the tropics. *A. G. B.*

Werner (H.). Zur Frage der Akklimatisation der weissen Rasse im tropischen Tieflande. [**The Question of Acclimatization of White Races in Tropical Lowlands.**]—*Deut. Med. Woch.* 1934. Mar. 30. Vol. 60. No. 13. pp. 478–481.

An article devoted chiefly to the German colonization of Espirito Santo, Brasil and to North Queensland.

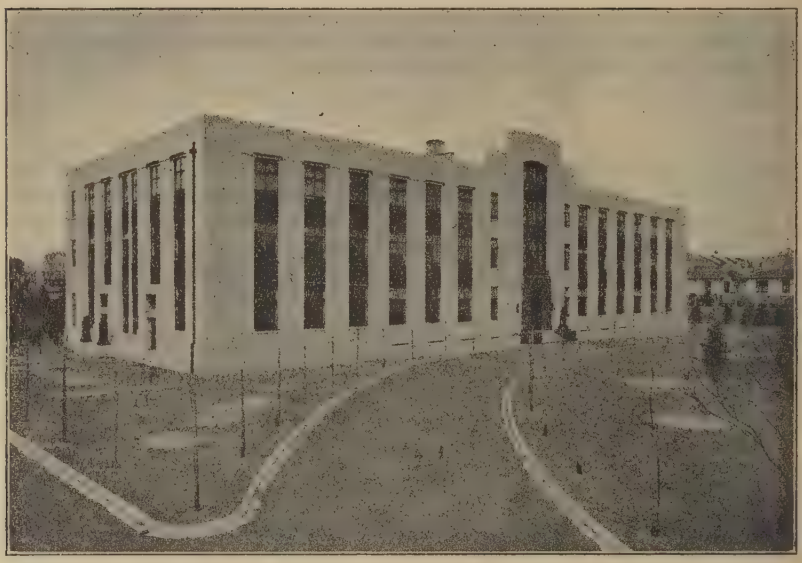
In the year 1847, 38 Rhenish families settled in Espirito Santo followed in 1857 [not 1897] by 280 families, in all about 1,000 persons. The birth-rate is given by Wagemann as 50–60 and the death-rate as 8–10 and the pure German population now numbers 17,000. The district settled lies between 17 and 22°S. on the eastern slopes of a mountain range. The average temperature is 20–21°C. Other data of temperature and precipitation are wanting but figures are given for the neighbouring town of Campos on the coast. The region is described as marginal tropics (Randtropen) and it is questionable how far it should be separated hygienically as it is by the geographers from the real tropics (Innentropen). It is noted that settlement began on the highest ground and gradually worked towards the plains [see this *Bulletin*, Vol. 15, p. 296–7].

After consideration at some length of N. Queensland experience the author expresses the opinion that given the absence of certain diseases, such as malaria, yellow fever and hookworm, provided that indigenous races are kept at a distance or kept free from infection and that muscular work is performed by the white settlers, acclimatization of white races in tropical lowlands is possible and attainable. *A. G. B.*

Henry Lester Institute of Medical Research.—56 pp. With 41 figs. & 7 plans. 1934. Shanghai.

This attractive brochure gives an account of the inception and organization of the Henry Lester Institute, Shanghai.

Henry Lester, who died in May 1926, had by will directed that there should be founded "such building or buildings as may be advisable for the establishment of an institute or institutes for the study of medical science, surgery, civil engineering, architecture and other useful and scientific knowledge." It was decided that there should be two separate institutes, one medical, the other technical, and that the medical institute should take the form of a post graduate organization with emphasis on research. The scheme for the establishment of the Henry Lester Institute for Medical Research was approved in May 1928 and in the following year heads of departments were appointed to work in temporary quarters. In 1932 it was agreed that the Institute should consist of three main divisions—Clinical Research; Physiological Sciences; and Pathological Sciences, and at the end of the year the new building was entered. A Department of Medical Statistics was also formed, its first function being the collection of reliable statistics of the incidence of disease in different parts of China.



The Henry Lester Institute of Medical Research, Shanghai.

The building is here described. It is built on three floors with a basement and follows the unit plan, *i.e.*, all rooms can be regarded as consisting of one or more units, the dimensions of which are 12 × 18 feet ; double units are 24 × 18 and so on, partitions being non-structural. Each floor is composed approximately of 40 units. The animal house is independent of the main building. The Director, Dr. H. G. Earle, discusses the organization of medical research. Dr. James Maxwell contributes a short article on the Library which has already 136 current periodicals. Other articles are by Dr. H. Gordon Thompson (Clinical Research and Experimental Surgery), Professor Bernard E. Read (Physiological Sciences) and Dr. R. Cecil Robertson (Pathological Sciences). The illustrations consist of plans and of views of the various rooms. The Lester Chinese Hospital, which houses the Clinical Unit, is also illustrated.

No information is given of the funds at the disposal of the Institute ; they must be assumed to be ample. A list is given of the scientific, and clerical and technical staff. *A. G. B.*

South African Institute for Medical Research. **Annual Report for the Year ended 31st December, 1933** [Lister (Spencer), Director].—91 pp. With 2 plates & 1 chart. Johannesburg : P.O. Box 1038.

A large laboratory like the South African Institute for Medical Research naturally deals with a great many subjects and comparatively few of these are essentially of tropical interest.

The concentrated plague serum prepared in the Institute was tested on rats and showed that none of the virtue of the serum had been lost in the manufacture. Value and concentration were exactly parallel, which is a very important finding. Plague vaccine was investigated from the point of view of preparation of an endo-anatoxin which may

possibly prove more efficacious than the ordinary vaccine. It would certainly be an important advance to have an effective vaccine which gave little or no inoculation reaction.

The Flexner type of dysentery which occurs locally and seasonally is ordinarily of a mild and transient type. Flexner-like bacilli were examined in considerable number. Their particular characteristics were that they gave the biochemical reactions of the group but were inagglutinable with standard Flexner sera. It is still to be determined how far they are really pathogenic.

Some work has been done on the standardization of T.A.B. vaccine where recently isolated cultures were used, being first plated and the smooth colonies selected. The white mouse was the test animal used and it is capable of being protected by the vaccine against multiple lethal doses of virulent strains. A method of vaccination which is becoming increasingly popular is the use of typhoid vaccine tablets taken orally with bile pills. Evidently the efficacy of this oral method is to be made the subject of statistical investigation.

Anatoxins have formed subjects of study and of use in one form or another for some considerable number of years. At the South African Institute the same principle of reduction of toxicity has been applied to snake venoms. The products are " anavenoms " and they are used with great success in the rapid preparation of concentrated antivenenes of high potency. A research of a comparative type of Indian and South African venoms and antivenenes " with particular reference to their toxicities, the detoxication of Indian venoms and the cross action exerted by the respective concentrated antivenenes upon heterologous venoms," should prove very interesting. It is time, for example, that an authoritative answer was given to the question whether the antivenene prepared to the venom of one snake is of any avail against the venom of any other species of snake.

These are merely one or two of the subjects of interest in this annual report for 1933. *W. F. Harvey.*

People's Commissariat for Public Health S.S.R.A. [**Proceedings of the 3rd Congress on the Campaign against Malaria and Other Tropical Diseases in S.S.R. of Armenia held at Erivan 5–9 March 1931.**]—164 pp. (State Publ. S.S.R.A., Med. Section) Erivan. 1933. [In Russian.] [4 roubles.]

This volume contains eighteen reports read at the above Congress. The majority (eleven) are on various aspects of malaria in the different districts of Armenia, such as incidence, economic importance, effect upon the population, prophylaxis, etc., and are of purely local interest. Amongst the remaining papers the following may be noted. According to Matevossian (p. 82) during the last few years 20 cases of *Balantidium coli* infection have been recorded from Armenia, in some of which contact with pigs could be definitely established. Tsaturian (p. 88) records 136 cases of acute and chronic amoebiasis during the period 1927–1930, the incidence being highest from the beginning of July to the end of September. Eolian (p. 113) draws attention to the wide distribution of echinococcosis in Armenia, which is associated with a high degree of infection in domestic animals (26 to 50 per cent. in dogs, 58 per cent. in cattle), and a low cultural level of the population living

in close contact with these animals. KARAPETIAN (p. 122) reports 18 cases of sprue between 1923, when the occurrence of this disease in Armenia was first recognized, and 1930. *C. A. Hoare.*

THOMSON (J. Gordon) & LAMBORN (W. A.). **Mechanical Transmission of Trypanosomiasis, Leishmaniasis, and Yaws through the Agency of Non-biting Haematophagous Flies. (Preliminary Note on Experiments.)**—*Brit. Med. Jl.* 1934. Sept. 15. pp. 506–509. [11 refs.]

The object of this preliminary note is to emphasize the important part which may be played by non-biting haematophagous flies in mechanical dissemination of blood-inhabiting organisms—a fact which appears hitherto to have been largely overlooked.

Most authorities are agreed that direct methods of infection by Tabanidae, Stomoxys, and other biting flies play an important part in the active spread of trypanosomiasis. Comparatively little work has been done on the transmission of the tissue-inhabiting pathogenic protozoa by Diptera other than biting species. CASTELLANI (1907) fed *M. domestica* on scrapings from yaws which contained *Treponema pertenue*, and afterwards, by transferring them to scarified sores on monkeys, produced an infection in one of the experimental monkeys. DARLING (1913) transmitted *T. evansi* to animals by means of house flies which infested the open sores on mules in Panama. LAVERAN (1880) suggested that oriental sore in Biskra might be due to transference of infection by flies, and WENYON (1926) stated that it was highly probable that the house fly which swarms round exposed oriental sores might sometimes carry the causative organism on its feet or proboscis to abrasions of the skin on another person; he likewise expressed the opinion that Leishmania bodies might pass rapidly through the gut of the fly and so be deposited with the dejecta.

In Nyasaland various species of muscids abound, and one in particular—*Musca spectanda*—has been shown by Lamborn to be almost entirely dependent on man throughout its whole life. The eggs are laid solely on human excreta, on which the larvae feed to maturity. The adult flies in the early morning settle on man, awaiting the opportunity to slake their thirst and deposit their eggs on his freshly excreted faeces. In one instance 35 female *M. spectanda* were captured in three-quarters of an hour from a linear scab half an inch long on the dorsum of the foot of a native.

It was these observations by Lamborn and the hypothesis put forward by him in 1932 concerning the part muscids may play in the spread, not only of trypanosomiasis, but also of cutaneous leishmaniasis, which led to the experimental work described in this paper. These experiments relate firstly to the mechanical transmission of *T. brucei* by *Musca spectanda*, secondly to the passage of living Leptomonads of the cultural forms of *Leishmania donovani*, *L. infantum*, and *L. tropica* through the intestines of *M. spectanda*; and thirdly to the passage of living *Treponema pertenue* through the gut of *M. spectanda*.

The authors summarize their results as follows:—

" 1. Non-biting haematophagous muscids feed readily to repletion on blood, serum, serous exudate, ulcers, sores, and also secretions from the nose, eyes, and mouth. After a meal a certain proportion

of these flies pass blood or serum in their numerous dejecta, which may contain large numbers of living trypanosomes, leishmania, or the *Treponema pertenue* of yaws.

" 2. These haematophagous flies have their preferred hosts—for example, *Musca spectanda* Wied, which occurs in great abundance in Nyasaland, favours man. It lays its eggs exclusively in human faeces, breeding very freely ; it derives moisture from human faeces, and could thus take up *L. donovani* from this source, since the organism is known to occur sometimes in this medium. Large numbers attack persistently and with determination scratches, cuts, and sores of the skin of man in search of food, and also haunt the eyes, nose, and mouth in search of fluid.

" 3. *Trypanosoma brucei* in the blood of rats and dogs are readily ingested by *M. spectanda*, and during a period varying between five minutes and six hours these flagellates can be passed alive in the numerous droplets of dejecta passed through the gut of the fly. Rats were experimentally infected by the intraperitoneal injection of these dejecta by placing a drop on a fresh cut on the ear and by placing the dejecta on a drop of blood exuding from the bite of a tabanid. *T. brucei* in the dejecta introduced into the eye, nose, and mouth did not produce infection. Certain flies after a feed extrude a drop of the ingested blood containing living trypanosomes from their proboscis five to ten minutes after a full meal.

" 4. Living leptomonads in cultures of *L. donovani*, *L. infantum* (dog strain), and *L. tropica* are freely ingested by *M. spectanda*, and are passed viable in the droplets of excreta for several hours after a feed. There can be no doubt that these flies could ingest the round tissue forms of all the human forms of leishmaniasis and pass them in a viable state either through the gut or by regurgitation from the proboscis to sores or mucous membranes. It would seem certain that both kala-azar and oriental sore could be actively transmitted through the agency of these flies.

" 5. *Treponema pertenue* of yaws passes rapidly in a viable form through the gut of *M. spectanda*, and so could easily be deposited on cuts and abrasions." *W. Yorke.*

CAZANOVE. Analyse de deux documents manuscrits du Docteur Peyre, Médecin-Chef de l'expédition de Saint-Domingue. [**Two Manuscripts by Dr. Peyre, Chief Medical Officer of the San Domingo Expedition.**]—*Rev. Méd. et Hyg. Trop.* 1934. Mar.–Apr. Vol. 26. No. 2. pp. 65–91.

An account of the mortal illness and autopsy of General Leclerc, Captain General of San Domingo, who died of yellow fever there in 1802. His wife was Pauline Bonaparte. One gets a glimpse of the high fatality. Between February and November 1802 there died 1,500 officers, 750 doctors, 25,000 soldiers, 8,000 marines, 3,000 seamen, 2,000 employees and 3,000 whites from France. " Of this number only 5,000 perished by war, yellow fever harvested the rest." Besides other documents and discussions the paper contains a memorandum on the health service of the Navy and Colonies by Dr. PEYRE, Inspector General. *A. G. B.*

MANAI (Andrea). Contributo allo studio delle associazioni morbose. Nota IIa. Sui rapporti tra malaria e tuberculosi polmonare. [**Association of Diseases. Relations between Malaria and Pulmonary Tuberculosis.**]—*Riv. di Malariologia.* 1934. Vol. 13. No. 4. pp. 443–473. [16 refs.] English summary.

The notion is fairly widespread that malaria and tuberculosis are mutually antagonistic ; that where malaria is epidemic tuberculosis is uncommon ; that malaria confers immunity against tuberculosis and that the malarious subject rarely contracts tuberculosis ; that malaria can be employed in the treatment of tuberculotics in that it slows down the tuberculous process and leads to fibrosis.

The author has lived and worked for many years in Sardinia where both diseases are widely spread, and he has been able to observe many persons who have presented, sometimes contemporaneously, sometimes consecutively, the symptoms of both infections. His experience is at variance with the opinions expressed above. He finds that recent malaria seemed to act adversely on the course of an existent tuberculosis, and in patients with tuberculosis who seemed to be making satisfactory progress on subsequently contracting malaria the disease appeared distinctly to be aggravated, as if the malarial infection weakened or handicapped the body's defences. He infers, naturally, that malariotherapy is not suitable for phthisical patients. *H. H. S.*

BOGGIAN (Bruno). Esiste veramente un antagonismo tra malaria e tubercolosi ? [**Are Malaria and Tuberculosis really Antagonistic ?**] *Riv. di Patol. e Clin. d. Tubercol.* 1934. July 30. Vol. 8. No. 6. pp. 513–517. [14 refs.]

For many years, from about the middle of last century, there has been a vague belief that paludism and tuberculosis were mutually antagonistic. The author's experience is totally at variance with this. He quotes in detail four clinical cases and according to his experience he finds that malaria appears to give rise to an anergic state as shown by the subsequent reaction to tuberculin, von Pirquet's or Trambusti's method. This anergy, though it may be but transient, is definite. Again, he has repeatedly observed that a malarial attack has been followed by tuberculosis, sometimes pulmonary, at others of the serous membranes. Lastly, he has almost constantly seen that in a tuberculous patient the supervention of malaria has resulted in the lighting up and extension of the tuberculous process already existing.

H. H. S.

YENIKOMSHIAN (H. A.). **Nonalcoholic Cirrhosis of the Liver in the Lebanon and Syria.**—*Jl. Amer. Med. Assoc.* 1934. Sept. 1. Vol. 103. No. 9. pp. 660–661.

In the author's experience hepatic disorders are common in Syria and the Lebanon, due to disease of the biliary tract, to hydatid and to amoebiasis, but apart from these is a group exhibiting hepatic enlargement with splenomegaly. It is with these last that the present article deals.

Many of the patients suffer from repeated febrile attacks with jaundice, transient enlargement of the liver, epigastric tenderness, nausea and vomiting, the attacks lasting perhaps for a few days only, but sometimes for weeks. The author found it more among farmers

and the rural population than among city dwellers, and mostly among those dwelling in villages near Tyre and Sidon.

During a period of six years he has seen in the wards 70 cases of portal cirrhosis with ascites ; about two-thirds of the patients were under 40 years of age, and 20 per cent. were under 20 years ; males affected were rather more than twice as numerous as females. Splenomegaly in most cases appears long before the ascites, and palpation reveals a hard, irregular liver which is enlarged to the end, and a large spleen and hobnail liver are seen at autopsy. [In temperate climates hobnailed liver with ascites is usually reduced in size.] The causation is obscure. The diet does not appear to be responsible. It is largely vegetarian and cereal ; mutton is eaten, beef, chicken and fish only occasionally. The men rarely and women never drink alcohol. Malaria and dysentery are common, as also are helminthic infestations, in order of prevalence, *Trichuris trichiura*, *Taenia saginata*, *Ascaris lumbricoides* and *Enterobius vermicularis*. Ankylostomiasis and filariasis are rare and there is no schistosomiasis. Syphilis is uncommon

The author is of the opinion from a prolonged study of these cases, both from the clinical and pathological aspects, that chronic malaria and amoebic dysentery, especially when combined, are important aetiological factors. *H. H. S.*

Gillan (Robert U.). **An Investigation into Certain Cases of Oedema occurring among Kikuyu Children and Adults.**—*East African Med. Jl.* 1934. June. Vol. 11. No. 3. pp. 88–98.

A condition is described in small children and in women having some of the characters of coeliac disease and sprue. A toxaemia of origin in the small intestine is suspected.

The author kept notes of 12 cases, seen in 2–3 years ; 9 in children all breastfed and 3 in women. There was generalized oedema, pallor, patchy desquamation of the skin and depigmentation of the hair ; the oedema was the chief feature and was sometimes so severe as to cause occlusion of the palpebral fissure ; there was no albuminuria. The children were extremely irritable and resented exposure. A history of 7–9 months illness was usual. Diarrhoea was usually noted. Blood counts indicated anaemia of varying intensity. The stools were large, pale, greasy or soapy looking, greyish and sour to the smell. Five patients died in hospital and possibly others outside.

The diganosis is considered in relation to coeliac disease, sprue, pink disease and beriberi. One stool was examined by a biochemist who reported a high percentage of saponified fat ; this is believed to be due to the diarrhoea and not to deficiency of biliary or pancreatic secretion. Histological examination revealed a severe chronic enteritis. Indications for further investigation are given. *A. G. B.*

Maegraith (Brian) ; McClosky (A. J.). **Pineapple Juice in Oedema.** [Correspondence.]—*Brit. Med. Jl.* 1934. Sept. 8 & 22. pp. 492 ; 572.

Dr. Maegraith mentions the case of a patient, a woman of 30 years, suffering from oedema of cardiac origin who had been treated by digitalis, mercurials, etc., but without success. The oedema affected back and legs and there was also double pleural effusion. She was given the

juice from a tin of pineapple daily and in a fortnight the oedema of trunk and legs subsided, the urinary output increased from 18–20 oz. to 60–100 oz. in the 24 hours, and in another week the pleural effusion cleared up. After leaving hospital she continued to eat one tin of pineapple a week and when she reported herself some months later she was still free from oedema.

Dr. McClosky follows the above communication by stating that in the course of an outbreak of beriberi in the gaol of Kuala Lumpur in 1896–98, the " Chinese patients with dropsy invariably asked for pineapple." He gave it as a placebo and the dropsy subsided, but unfortunately for the test they were given other diuretics also. He mentions that Chinese patients with wet beriberi in other State Hospitals also used to ask for pineapples. The treatment is worth further study.

H. H. S.

MONCRIEFF (Alan) & WHITBY (L. E. H.). **Cooley's Anaemia.**—*Proc. Roy. Soc. Med.* 1934. Aug. Vol. 27. No. 10. p. 1324 (Sect. for Study of Disease in Children p. 56).

—— & ——. **Cooley's Anaemia.**—*Lancet.* 1934. Sept. 22. pp. 648–649. With 1 chart.

The case here described would formerly have been classed as von Jaksch's anaemia, but the conditions present several differences from the latter as understood by English paediatricians. Attention was first drawn to it by T. B. COOLEY, an American physician, in 1927. The patient is nearly always of Mediterranean stock ; the subject of the present article was a girl of 1½ years old born in the Middlesex Hospital of Greek parents. The findings were typical : erythrocytes in the neighbourhood of 3 million per cmm., Hb. 38–40 per cent., leucocytosis about twice the normal. The biochemical investigations are detailed in the report to which those interested should refer. Radiographically, all the bones showed generalized rarefaction ; the skull bones thinning of the tables and increase in medulla. Post mortem the skull bones were very soft, and the bony tissue of the femur very thin, with marrow a dense dark red. The spleen was a little enlarged as was also the liver. The condition has been named Cooley's anaemia from the physician who first described it ; another name is " thalassaemia " on account of its predilection for the Mediterranean races. *H. H. S.*

MCROBERT (George R.). **The Treatment of Bacterial Food Poisoning.**—*Brit. Med. Jl.* 1934. Aug. 18. pp. 304–305.

The author has abandoned the use of purgatives in bacterial food poisoning, so common in the tropics and now relies entirely on the absorptive action of kaolin, preferably a preparation of " colloidal " kaolin, which serves to detoxicate the bowel while soothing and protecting its lining. In a severe case treatment by rest in bed with warm bottles, gum-saline or Rogers' hypertonic saline is supplemented by the oral administration of 2 drachms to the wineglassfull of kaolin, after which morphine may be injected without harm. One drachm of kaolin is advised every 15 minutes until the diarrhoea is controlled. In less severe cases frequent kaolin and large quantities of water are advised. The author regards the introduction of fine kaolin as one of the most important recent advances in practical everyday therapeutics.

A. G. B.

Palmer (F. J.). **Hot Weather Ear—a Clinical Entity.**—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 430–432.

This is a condition seen in soldiers in Assam and elsewhere in India in which the ear becomes painful, the meatus is more or less blocked by swelling and a ring of skin eventually separates. The treatment is described. The author suggests it is a ringworm infection with probably a bacillary one added. Most cases occur in the hot weather.

A. G. B.

Noosten (H. H.), Kirschner (L.) & Vos (J. J. Th.). Rhinoscleroom op Bali. [**Rhinoscleroma on Bali Island.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. July 3. Vol. 74. No. 14. pp. 835–852. With 1 fig., 1 map & 51 figs. on 4 plates.

A focus of rhinoscleroma had been described upon the island of Samosir in the Toba lake, Sumatra (this *Bulletin*, Vol. 30, p. 49) and the view promulgated that this was a disease of primitive people. Now a new focus has been found by the authors upon the island of Bali.

The disease, which is infectious, has its seat in the respiratory tract and may occur anywhere from the nares to the hilum of the lung. It is an infiltrative condition, slowly and continuously progressive, without necrosis or ulceration and is terribly disfiguring. A causal organism, one of the capsule bacilli, is found and can be distinguished from the pneumobacillus and the ozaena bacillus by serum tests. Histologically the scleromatous tissue is found to be permeated with plasma cells but most characteristic of the condition are the so-called cells of Mikulicz, which are in all probability swollen and degenerated endothelial cells. As a culture medium for the bacillus, Drigalski agar is better than ordinary agar, for then the growth of cocci and of proteus bacilli is inhibited. Nine clinical cases are described as being typical, although there were others which were almost certainly also cases of rhinoscleroma. A differential diagnosis by histological, bacteriological and serological means could be made of the affection from nasal polypi, chronic inflammations of the nasal accessory sinuses and from pathological processes due to syphilis, yaws and leprosy. The authors do not think that these cases are restricted to northern Sumatra and Bali and they expect that reports of their occurrence will in due course be forthcoming from Java and other places. Therapeutic measures range over autovaccines, protein therapy, artificial malarial infection and gold preparations but the most favoured method of treatment is by irradiation, although it may be followed by unpleasant complications.

W. F. Harvey.

Castellani (Aldo). **Elephantiasis Nostras (Non-filarial Elephantiasis).** —*Proc. Roy. Soc. Med.* 1934. Mar. Vol. 27. No. 5. pp. 519–523 (Sect. of Trop. Dis. & Parasit. pp. 25–29).

The cases described were contracted in non-filarial countries—Great Britain, Italy, the Balkans and parts of the United States, and their elephantiasis is held to be of bacterial origin.

For detection of bacteria the lymphatic glands must be examined, and this must be done when lymphangitis and lymphadenitis are actually present. The organisms are of 4 groups, gram-positive staphylococci probably of little aetiological import, gram-positive streptococci

mostly of haemolyticus type, gram-negative *Micrococcus myceticus* which are more likely to produce slowly developing abscess or sinus than elephantiasis, and *M. metamyceticus* whose subcultures may vary in their staining reaction. The sequence of pathological change is—acute bacterial lymphangitis and lymphadenitis usually starting from some small lesion, perhaps an epidermophytic crack, oedema at first fluid and then solid, and hyperplasia of skin and subcutaneous tissue. During acute lymphadenitis, the enlarged and congested gland shows many thickened and perhaps thrombosed vessels, with the lymphoid tissue but little changed; later there is fibrosis with atrophy of this tissue. The main changes in the dermis are—lessened bulk of individual epithelial cells with loss of prickles and corresponding approximation of nuclei, and many dilated lymph spaces, thickened arterioles, and fibrosis; symptomatology and site are as for filarial elephantiasis and the condition is progressive. Diagnosis depends on place of residence and antigen-based tests. In the acute stages well-diluted salicylates are advised, 10 to 15 grains [0·6 to 1 gm.] thrice daily; in the chronic, weak vaccine doses 10 to 100 millions every 4th or 5th day; in the pachydermatous stage, a month in bed half-yearly with bandaging and fibrolysin injections. Any operation should be preceded by a vaccine course.

In discussion MANSON-BAHR classified the causation. MACCORMAC quoted HANDLEY'S opinion that lymphatic obstruction will not alone cause elephantiasis, but that the resultant fibrosis will obstruct neighbouring veins. Parkes WEBER alluded to the congenital group. Hamilton FAIRLEY stressed the focal nodes of filarial elephantiasis and the intradermal test as distinguishing the two forms of the disease.

Clayton Lane.

MORALES-OTERO (P.) & POMALES-LEBRÓN (A.). **Antistreptolysin Content of Sera from Cases of Recurrent Tropical Lymphangitis.**—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1170–1172.

A contribution from the School of Tropical Medicine, University of Porto Rico. The antistreptolysin values of the sera of 41 patients suffering from recurrent tropical lymphangitis and of 20 normal subjects are reported. The antistreptolysin titre is increased in the former series: here 3-figure values are usual, in the normal subjects they are rare. The serum of two acute lymphangitis cases varied in antistreptolysin titre before, during and after the attack. *A. G. B.*

REVIEWS AND NOTICES.

KOLLE (W.) [Director, Inst. Experim. Therap. & Chemiotherapeutical Res. Inst., " Georg Speyer-Haus," etc.] & HETSCH (H.) [Professor Inst. Experim. Therap., Frankfort]. **Experimental Bacteriology in its Applications to the Diagnosis, Epidemiology, and Immunology of Infectious Diseases. Vol. 1.** [Edited by John EYRE, F.R.S. Edin., F.Z.S., M.D., M.S., D.P.H., Director Bact. Dept., Guy's Hosp., etc.]—592 pp. With 118 plates & 200 text figs. 1934. London: George Allen & Unwin Ltd., 40 Museum Street, W.C.1. [30s.] [Review appears also in *Bulletin of Hygiene.*]

This is the first volume of the translation of the well-known and standard German text-book " Experimentelle Bakteriologie " by Kolle and Hetsch. The work has already reached a seventh German edition and has been translated into several languages. Originally based on lectures to University students it is refreshingly free from the faults of compression. Though it makes a somewhat large book it is easy to read continuously and with interest, a rather unusual feature in bacteriological text-books. It is based more than most modern text-books on tradition and it is most sound and interesting when on the older and well beaten tracks of bacteriology. Any teacher or student of bacteriology would profit by reading " Kolle and Hetsch " if only because it gives an excellent idea of the best German teaching, but it has an appeal to more specialized classes of readers. Both the student of clinical medicine and of public health may obtain an excellent general idea of what bacteriology has accomplished in those spheres, and what is still more valuable—an idea of how the bacteriological outlook may illuminate other branches of medicine. Over and above the general treatment there are several chapters of special excellence. The account of cholera, typhoid, anthrax and many other diseases could hardly be bettered as single chapter accounts, not merely as bacteriology but as general descriptions of those diseases.

To students of tropical medicine the book is particularly adapted, not only for the wealth of information it provides on infective (including protozoal) disease but also because it illustrates so admirably a point of view absolutely necessary to the tropical practitioner, that no line can be drawn between clinical and laboratory knowledge. The numerous illustrations, many of them in colour, which have been such an admirable feature of the German versions are beautifully reproduced. The translation of such a work is a formidable undertaking which on the whole has been carried out satisfactorily. The inevitable typhus for typhoid has been allowed to escape in one or two places. And in such chapters as that on gas-gangrene not enough trouble has been taken to link up English and German nomenclature. These are, however, but small faults in an otherwise admirable version. *C. C. Okell.*

KNOWLES (R.). **The Calcutta School of Tropical Medicine 1920–1933. An Essay-Review.**—*Supplement to Ann. Rep. of the School for 1933.* pp. 168–xlvii. 1934. Bengal Govt. Press.

Col. Knowles, who was concerned with the Calcutta School in its prenatal days, who officiated at its birth and has been intimately connected with it ever since, is eminently fitted to describe its early

development and the result is worthy of his facile pen. It starts with a brief review of the financial and administrative difficulties which surrounded its inception, and he gives full recognition to the energy and enthusiasm of Sir Leonard ROGERS, who is in fact the founder of the School, and also to the influence exercised by its successive directors, Sir John MEGAW and Lt.-Col. H. W. ACTON. It is a particular cause for congratulation that generous financial support came from some of the Calcutta business community, and the fact that their support is still being maintained in spite of economic depression augurs well for the continued co-ordination of science and industry founded on reciprocal benefits. Col. Knowles gives a short account of the work of the School as a centre for post-graduate training in tropical diseases and in public health. Though his reference is brief it is questionable whether this is not the most important of the School's activities in view of the fact that the safeguarding of India's public health will, in the near future, lie largely in the hands of the rising generation of Indians.

The third part of the review deals with work past, present and future of the major researches carried on at the School and to this part tropical workers will naturally turn.

Of their many successes we may make special mention of the *kala azar* problem, particularly the part played by the sandfly and the preparation and testing of the antimony compounds as well as of the careful epidemiological observations thereon. The use of the pentavalent antimony compounds represents one of the most dramatic and successful therapeutic discoveries of the century and in this triumph the Calcutta School can rightly claim a share.

Valuable work has been done in *malaria*, particularly that concerned with the disease in monkeys, which is another of Knowles' personal successes. The discovery of an animal susceptible to a disease is always the key-point in its elucidation and so it comes that the transmission of human malaria under controlled conditions and of monkey malaria has already thrown more light on the problems of malaria and blackwater fever than a generation of laboratory and field work had been able to accomplish.

The *dysenteries* have received a good deal of attention without there being much progress to record, whilst regarding *sprue*—well, anyone who still entertains any lingering doubt regarding the pathogeny of this mysterious disease should now have his doubts dispelled, so simple does it all appear !

Cholera research largely resolves itself into a consideration of the bacteriophage problem, the complexity and controversial nature of which is well known. The relation between agglutinable and non-agglutinable vibrios is still unsettled and according to these researches this is dependant on the permutations and combinations of ten specifically different bacteriophages. Despite this confusion " the manufacture of bacteriophage for Government hospitals is now an important part of the work." " Trying it on the dog " with a vengeance ! The section on *hookworm* and *filariasis* is comprehensive, and LLOYD's observations on the complement fixation reaction in the latter disease are interesting. He shows that some cases give a positive reaction together with eosinophilia whilst others show a negative reaction with a polymorphonuclear increase, suggesting that local sepsis conceals or destroys the antigenic reaction due to the presence of the worms. The work of MUIR on *leprosy* has brought much credit to the Calcutta School, but despite the volume of work performed here

and in other parts of the world we are still unable to determine the actual curability of this disease. It is good to learn that of a number of remedies, hailed with enthusiasm and abandoned with regret, some remain which give promise of more permanent value.

The Calcutta workers themselves have helped to tone down the extravagant optimism of twenty years ago and to show that the building up of the lepers' resistance and the treatment of intercurrent disease has as least as much value as the use of any particular drug. Space does not permit a detailed reference to other subjects of major research namely epidemic dropsy, lathyrism, diabetes, spirochaetoses, the indigenous drugs and the drug addiction enquiries, and diseases of the skin and respiratory system.

The fourth division of the Essay-Review is taken up by departmental reports and the work undertaken by each in chronological order. There is necessarily a good deal of repetition and overlapping in this part of the review, but it contains much interesting routine work and the record of minor researches which have been essayed but not brought to maturity.

MEGAW's description of tick typhus in India is an outstanding contribution to the Tropical Medicine Section and is one of the few major contributions to purely clinical medicine.

Col. Knowles ends his 168 pages with a brief note regarding the " future " and one is glad to find that his superabundant optimism still holds and is an answer to those who experience " that sinking feeling " when contemplating the full Indianization which approaches so rapidly. Col. Knowles with his gift (almost one might write " urge ") for self expression has carried out the analyses of the School's activities (together with that of 740 original papers) in the true Boswellian spirit. He deserves well of his School whilst the rest of us will be grateful for his description of the work of this already distinguished institution.

F. P. Mackie.

HEGLER (C.) & NAUCK (E. G.). Tropenkrankheiten. [**Tropical Diseases.**]—Reprinted from MOHR & STAEHELIN's *Handbuch der inneren Medizin.* Dritte Auflage. Erster Band. Infektionskrankheiten. pp. 1098–1212. With 67 figs. (14 coloured).

Within the limits of about a hundred pages Drs. C. Hegler and E. G. Nauck, of Hamburg, describe the following diseases : malaria, blackwater fever, relapsing fever, rat-bite fever, sleeping sickness, kala azar, Chagas's disease, dengue, papataci fever, Japanese river-fever and yellow fever. Of these diseases the only ones that are dealt with at all fully are malaria, blackwater-fever and yellow fever ; but in the descriptions of the other subjects, though they are necessarily very compressed, very little of importance seems to have been omitted. The accounts given of the pathology and morbid anatomy of the various diseases are especially good, and the illustrations, many of which have been borrowed from other books, have been carefully selected and are very satisfactory. As there are already in existence several excellent German books on Tropical Medicine, it is presumably for the sake of completeness that this section forms part of the first volume of the large work on Medicine founded by Drs. Mohr and Staehelin : the authors show such a practical firsthand knowledge of their subject that one cannot help regretting the limitation of space imposed upon them.

H. J. Walton.

ROCKEFELLER FOUNDATION. **Annual Report 1933** [MASON (Max), President].—pp. xix+477. With 40 illustrations. New York: 49 West 49th Street. [Review appears also in *Bulletin of Hygiene.*]

In a foreword to this report, the president states that " the Foundation is dedicated to the welfare of mankind," and it is certainly in this spirit that its many activities are carried on. Wherever there is need of it, in both hemispheres of the world, substantial help is given to any undertaking which is working to promote improvement in Public Health or useful knowledge. During the year 1933 demonstrations of the practical application of various health measures were given in many countries; and funds were provided for the establishment of public health laboratories, for resident and travelling fellowships, for training in midwifery, nursing, sanitary engineering and other cognate subjects. In China and in Java the Foundation representative is adviser to the Government; in the former country he is also professor of hygiene, and Head of the department of public health at the Peiping Union Medical College. As the report says: "the Foundation is not committed to any one country or place. It can follow a problem wherever that problem develops, and thus gain experience in handling situations under a great variety of conditions."

Those parts of the report which deal with public health and medical science describe much research work both in the laboratory and the field.

An extensive survey was made in 1933 of the areas in Africa in which yellow fever occurs. This was facilitated by the discovery that *Macacus rhesus* and white mice are susceptible to the disease, and by the application of the " protection test " (*i.e.*, the ability of the blood-serum of a person who has recovered from yellow fever to protect mice from infection). It was found that yellow fever in a mild form may exist for years as an undetected disease. In French Equatorial Africa, where yellow fever had never been reported, over eighteen per cent. of the blood specimens collected in thirty-seven towns, both on the coast and in the interior, protected white mice against the virus. As in former years, the Foundation has worked at the control of yellow fever in Brazil. In that country a system of routine microscopic examination of liver-tissue, from persons who had died after brief febrile illnesses, was found to be very effective in the detection of unsuspected cases of yellow fever.

Much antimalarial work was done in many places. Extensive mosquito surveys were made in the Amazon valley, the Philippines, Greece, Panama and elsewhere. A certain strain of a plasmodium from the canary (*P. cathemerium*), obtained from Rome, was maintained for ten months by bi-weekly passages, during which time it failed to produce any gametocytes, though another strain from the same source continued to produce the sexual forms of the parasite.

From the study of dogs, infested with *Ancylostoma caninum*, it appears that the anaemia is not caused by any special toxin; it results from direct haemorrhage, and responds well to treatment with iron. Seven cases of acute hookworm disease were observed at Porto Rico; the disease seems to have been contracted by bathing in highly polluted seawater. The symptoms came on suddenly, with dermatitis followed by much discomfort in the throat; within two to four weeks, colic and diarrhoea appeared. The patients were unusually weak, pale, and lost weight rather rapidly. A description is given of a larval variety of

hookworm disease, characterized by loss of strength and weight, anaemia, irregular fever, high eosinophilia and leucocytosis. There are few, or even no worms at all, in the intestine, and, in the latter case, absence of ova in the stools; the diagnosis may be difficult. It is thought that, in such cases, only a few larvae have been able to reach the intestine, the others remaining in the tissues of the body.

Research and routine work were done in many other tropical diseases besides those already mentioned.

The annual Report of the Rockefeller Foundation is always interesting, and the interest is fully maintained in that for the year 1933. The work is evidently carried on with great enthusiasm, and it owes much of its success to the admirable organization at the Centre.

H. J. Walton.

PITTALUGA (Gustavo). El tratamiento del paludismo. [**The Treatment of Malaria.**]—96 pp. [9 pages of refs.] Coleccion de Monografias de "Los Tratamientos Actuales." 1934. Madrid. [250 pesetas.]

This is the first of a projected series of monographs on modern treatment, and if the others are as good as this the series will be a valuable one. In a handy little volume of 100 pages the most recent views on the treatment of malaria are presented. Professor Pittaluga deals with the subject under the following headings: (1) The acute primary attack, subtertian, benign tertian and quartan; (2) Recrudescence and relapse; (3) Chronic and latent infections; (4) Anomalous forms, mixed infections, haemoglobinuric fever, quinine idiosyncrasy, etc. He devotes a chapter to experimental malaria and a pharmacobiological study of new drugs. Having considered each of these in detail, the author devotes a final chapter to a summary and recapitulation. The work concludes with a good selective bibliography of nearly 100 references of which more than one-third are British. *H. H. S.*

WENCKEBACH (K. F.). Das Beriberi-Herz. Morphologie. Klinik. Pathogenese. [**The Beriberi Heart.**]—(Pathologie und Klinik in Einzeldarstellungen, Bd. vi.) pp. vi+106. With 38 figs. 1934. Berlin & Vienna. Verlag von Julius Springer. [Rm.12; Bound 13·50.]

The observations recorded in this monograph were made by Professor Wenckebach a few years ago in the Dutch East Indies and Singapore. He was able to conduct post-mortem examinations on a number of cases of beriberi, and taking the precaution of injecting a hardening fluid shortly after death he confirmed the presence of certain gross anatomical changes as characteristic of the disease. These changes were for the most part demonstrable during life by means of radiography. The whole of the right side of the heart, including the conus arteriosus, was always greatly enlarged while the left side remained comparatively small. The large systemic veins were enormously distended; as much as 3 litres of blood sometimes escaped from incisions made in the region of the right auricle. The extra-pericardial pulmonary vessels on the other hand were not abnormally congested. Microscopic examination of the heart muscle after death revealed changes of the nature of intracellular oedema, sarcolysis, hydropic degeneration and so on. These changes were by no means constant,

hence it did not seem likely that primary changes in the efficiency of the heart muscle could explain the entire clinical picture of heart failure in beriberi.

The clinical signs in well developed cases were cardiac enlargement, murmurs, often inconstant and transitory, a rapid bounding pulse, enlarged liver and congested veins, a normal or raised systolic blood pressure with a low diastolic pressure and swelling of the calves without visible oedema. The clinical picture suggested that abnormalities in the peripheral circulation might be responsible in part for the heart failure. This suggestion received support from the observed results of injections of adrenalin and pituitrin. In convalescent cases adrenalin produced a striking return of the signs and symptoms, causing an increase in the venous pressure and pulse rate and a lowering of the diastolic blood pressure. These effects were interpreted as being due to a dilatation of peripheral arterioles leading to a sudden flooding of the right side of the heart. Pituitrin, on the other hand, had exactly the contrary effect, causing a fall in venous pressure and pulse rate and a raising of the diastolic blood pressure ; at the same time the subjective symptoms were greatly improved. These effects were ascribed to an increase in the tone of peripheral arterioles.

In his summing up the author puts forward the hypothesis that the primary cardiac lesion in beriberi is a loss of contractility of the heart muscle, possibly related to increased water retention within individual muscle fibres. Associated with this cardiac lesion is a loss of peripheral vascular tone which intensifies the signs and symptoms of cardiac insufficiency. The possible rôle of ductless gland disturbances in bringing about the cardio-vascular changes is considered worthy of further investigation. *S. J. Cowell.*

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